THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—21ST YEAR. SYDNEY, SATURDAY, APRIL 7, 1934. No. 14.

Table of Contents

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— PAGE.
"Studies in the Composition of the Gastric Juice", Part II, by G. V. RUDD, M.Sc. 455
"Observations on Hæmochromatosis", by KEMPSON MADDOX, M.D., M.R.C.P., and E. BEATRIX DURIE, B.Sc., M.B., Ch.M. 463

REPORTS OF CASES—
"Erythrœdema Polyneuritis (Pink Disease)", by JAMES H. YOUNKMAN, M.B., B.S. 473
"Unusual Blood Sugar Curves", by BRUCE HUNT, M.D., M.R.C.P. 474

REVIEWS—
Vaccine Therapy 474
Biological Chemistry 474

LEADING ARTICLES—
Broadcasting and Medicine 475

CURRENT COMMENT—
Pain as an Index of Disease 476
A Journal Devoted to Leprosy 477
An Example to Hospitals in New South Wales .. 477

ABSTRACTS FROM CURRENT MEDICAL LITERATURE— PAGE.
Medicine 478

SPECIAL ARTICLES ON TREATMENT—
The Treatment of Ingrown Toe Nail—Ingrowing Toe Nail—Paronychia 480

BRITISH MEDICAL ASSOCIATION NEWS—
Scientific 481

OBITUARY—
Thomas William Sherlock Mason 484
Robert Kingsbury Lee-Brown 484

CORRIGENDUM 484

MEDICAL APPOINTMENTS VACANT, ETC. 484

MEDICAL APPOINTMENTS: IMPORTANT NOTICE 484

EDITORIAL NOTICES 484

STUDIES IN THE COMPOSITION OF THE GASTRIC JUICE.

PART II.

By G. V. RUDD, M.Sc.,
Biochemist, Institute of Medical Research, Royal North Shore Hospital of Sydney.

FROM the time of the publication of the first analyses which attempted to establish a chemical basis upon which theories of the nature of gastric juice might be founded, this aspect of gastric digestion has continued to be the subject of investigation. The many substances present in gastric juice have frequently not been considered individually. Indeed, it has been customary to consider them in such groupings as free hydrochloric acid, total acidity, total chloride and neutral chloride, although a clear conception of what such groupings signify has not invariably been held by all investigators. The complex composition of the fluid that may be removed from the stomach, even when it is uncontaminated with non-gastric secretions, is itself an obstacle to the understanding of the conditions under which it was secreted. Variations in composition of the fluid which occur as a result of changes in the experimental conditions and the interpretations of these variations are responsible for the present-day differences between theories of the nature of the secretions of the stomach. Such theories may conveniently be considered in four divisions.

First, the work of Pavlov[16] led him to conclude that acid at the moment of its secretion is produced at constant concentration. At the beginning of secretion partial neutralization of acid is effected by "alkaline gastric mucus" on the walls of the stomach. At a high secretory rate the neutralization is much less than when the secretion is sparse. In active secretion, after preliminary neutralization

of the "alkaline gastric mucus" has occurred, the gastric juice is regularly and strongly acid, whether quickly or slowly secreted. Therefore, the end of secretion is characterized by the absence of the low acidity which is noted at the beginning. A development to this theory was added by Boldereff.[1][2] He said that when acidity of the fluid in the stomach is high, for example, 0·5% hydrochloric acid, partial neutralization must occur before the fluid is acceptable to the intestine. Regurgitation of alkaline duodenal fluid into the stomach effects this neutralization. This "self-regulation of the acidity of the contents of the stomach" results in the reduction of the high constant acidity of the freshly secreted acid to a level of 0·15% to 0·20%.

Secondly, the theory of Rosemann[17] must be considered. He regards gastric secretion as occurring in two phases: (i) The secreting cell receives "body fluid" of known total chloride content constantly throughout a period of secretion. (ii) To what extent hydrochloric acid is separated from this fluid and how much unchanged chloride appears in the gastric juice depends upon the secretory energy of the cell. The secretory energy falls towards the end of the production of gastric juice; therefore the hydrochloric acid falls and the neutral chloride rises. What is constant, within narrow limits, is not the hydrochloric acid, but the total chloride. Rosemann's conclusions were based upon careful work and the most complete analyses which had been done up to that time. In all his work, however, only one dog was used, the "sham-feeding" method being employed.

Thirdly, MacLean and his collaborators[14][15] have advanced Rosemann's theory to the ultimate limit. They believe that under the conditions which they established the stomach could secrete a fluid containing no hydrochloric acid, but neutral chloride in a fixed concentration which is approximately that of the chloride of blood. Their value for the constant chloride for human subjects is about 0·11 normal (0·39%), which is different from their own[15] and from Rosemann's[17] value for dogs, which is approximately 0·17 normal (0·60%). They agree, qualitatively at least, with Rosemann that the total chloride and not the acidity is constant in gastric juice. These views have met with much opposition. Boldereff,[3] in particular, accuses MacLean and his colleagues of attempting "to revive the long-dead corpse" of the *"Verdünnungssaft"* (diluting juice). Unbiased consideration of MacLean's results, however, does lead to the conclusion that in the abnormal conditions which he established secretion of a neutral chloride solution did occur. But which of the gastric glands produced this fluid remains quite obscure.

Fourthly, consideration of much more recent work than that of Pavlov and of Rosemann shows that a number of investigators believe that the most important characteristic of the secretion of the parietal cells is that it has constant or nearly constant acidity. The continued secretion of "alkaline mucus" is held to be largely responsible for changes observed in the acidity of successive specimens. Thus Bolton and Goodhart[4] conclude that the acidity of the secretion is often constant, but that at the beginning and the end of secretion there frequently occurs "an escape of neutral chloride at the expense of acid". Further, they attribute to the "alkaline mucus" secreted by the body of the stomach some slight acid-neutralizing powers. Webster[21] adopts what is essentially the same point of view. Hollander and Cowgill[11] press the conception further in stating that no fluctuations at all occur in the acidity of the secretion of the parietal cells. What variations occur in the acidity of fluid in the stomach are due to the neutralizing and diluting effect of gastric mucus. Hollander[10] regards gastric juice as a mixture of "parietal secretion"—a solution of hydrochloric acid isotonic with the blood—and "mucous secretion" which contains bicarbonate, neutral chloride and fixed base. McCann[13] has reached conclusions similar to Hollander's.

Briefly, then, the controversy concerning the nature of gastric secretion has chiefly been concerned with the questions: (i) Is hydrochloric acid secreted by the parietal cells at constant or variable concentration? (ii) If it is variable, what are the limits to its variations? (iii) What part do secretions of cytological elements of the gastric glands, other than the parietal cells, play in regulating the acidity of the gastric juice?

The experimental methods outlined in the previous paper[19] for the study of the composition of the gastric juice have been used in obtaining the data which will be discussed in the present work. The bearing that the results have upon the above questions will be considered after the statement of the results.

Experimental Results.

In Tables I to V are given the analyses of series of specimens of gastric juice obtained from several subjects according to the technique outlined in Part I of this paper.[19] Since acid was estimated always as described there, the customary estimations for free hydrochloric acid and total acidity are replaced by one value which is considered to represent the hydrochloric acid present. All the substances estimated are expressed in terms of milliequivalents per litre. The arrangement of results really represents the customary calculation of neutral chloride as the difference between total chloride and acidity, with the exception that here the neutral chloride is calculated as the sum of total chloride and inorganic phosphate *minus* the acidity. With this quantity thus corrected for phosphate is compared the sum of the bases present, each of the latter having been estimated separately. In the tests with subjects III and IV (Tables III and IV) the first specimens of gastric juice collected appeared fairly rapidly and were strongly acid. These subjects were not given an injection of histamine. With

TABLE I.
Analysis of a Series of Specimens from Subject I.
(The results are stated in milliequivalents per litre.)

Substance.	Specimen Number.					
	1	2	3	4	5	6
Sodium	42·70	39·40	24·70	13·26	21·46	38·20
Potassium	15·44	16·83	15·83	14·36	12·67	12·88
Calcium	3·40	3·67	3·68	2·50	2·42	2·98
Magnesium	1·02	1·88	1·81	2·48	1·85	1·86
Ammonium	10·60	9·98	9·14	7·88	10·14	10·14
Total base	73·16	71·76	55·16	40·48	48·54	66·06
Total chloride	65·0	76·2	105·8	108·2	105·8	87·6
Phosphate	3·32	3·00	1·28	1·15	1·56	2·14
Sum of total chloride and phosphate	68·32	79·2	107·08	109·35	107·36	89·74
Acid	0	6·94	51·00	69·80	58·90	22·50
Neutral chloride	68·32	72·26	56·08	39·55	48·46	67·24

Specimen Number 1 was collected during 30 minutes, and specimens Numbers 2 to 6 each during 15 minutes. Histamine (0·5 milligramme) was injected at the end of collection of specimen Number 1.

subjects I and II (Tables I and II) histamine was injected after the first specimen had been collected during a period of thirty minutes. With subject V (Table V) two specimens were obtained before the injection of histamine was given.

TABLE II.
Analysis of a Series of Specimens from Subject II.
(The results are stated in milliequivalents per litre.)

Substance.	Specimen Number.					
	1	2	3	4	5	6
Sodium	49·50	38·20	22·86	10·61	12·13	39·60
Potassium	16·83	14·07	14·07	12·58	10·89	14·75
Calcium	3·27	2·88	2·76	2·17	2·62	3·27
Magnesium	0·90	1·55	1·66	2·35	2·13	1·94
Ammonium	0	0	0	0	0	0
Total base	70·00	56·70	41·35	27·71	27·77	59·56
Total chloride	66·2	109·9	138·0	137·0	128·5	81·0
Phosphate	2·90	2·58	1·50	1·05	1·16	2·26
Sum of total chloride and phosphate	69·10	112·48	139·50	138·05	129·66	83·26
Acid	0	54·5	100·0	110·9	102·0	22·26
Neutral chloride	69·1	57·98	39·5	27·15	27·66	61·00

Specimen Number 1 was collected during 30 minutes, and specimens Numbers 2 to 6 each during 15 minutes. Histamine (0·5 milligramme) was injected at the end of collection of specimen Number 1.

Discussion of Results.

Acidity and the Neutral Chloride.

The anion present in preponderating amount in gastric juice is chloride. Bicarbonate is present in anacid specimens. Inorganic phosphate occurs in very small amounts, which are comparable to blood inorganic phosphate, but no other anions are present

TABLE III.
Analysis of Two Successive Specimens from Subject III.
(The results are stated in milliequivalents per litre.)

Substance.	Specimen Number.	
	1	2
Sodium	30·20	25·93
Potassium	10·80	12·00
Calcium	4·32	3·48
Magnesium	3·67	3·88
Ammonium	2·16	2·28
Total base	51·15	47·57
Total chloride	105·0	115·0
Phosphate	2·85	2·94
Sum of total chloride and phosphate	107·85	117·94
Acid	56·50	69·80
Neutral Chloride	51·35	48·14

Specimen Number 1 (19 cubic centimetres) was collected in 25 minutes, and specimen Number 2 (16 cubic centimetres) in 16 minutes.

in appreciable quantity. Therefore, the sum of the anions, chloride and phosphate, *minus* the acid, will represent the anion equivalent to the non-acid cations present. In other words, this quantity is the neutral chloride corrected for phosphate. Now the neutral chloride may also be found by taking the sum of the cations other than hydrogen ion, that

TABLE IV.
Analysis of Three Successive Specimens from Subject IV.
(The results are stated in milliequivalents per litre.)

Substance.	Specimen Number.		
	1	2	3
Sodium	16·19	23·57	23·00
Potassium	12·08	12·87	15·44
Calcium	2·43	2·29	2·49
Magnesium	2·08	1·24	1·95
Ammonium	2·00	2·00	2·31
Total base	34·78	41·97	45·19
Total chloride	99·4	87·6	107·8
Phosphate	1·76	1·52	1·52
Sum of total chloride and phosphate	101·16	88·52	109·32
Acid	66·3	45·5	65·9
Neutral chloride	34·86	43·02	43·42

Collection times: Specimen Number 1 (26 cubic centimetres)—20 minutes; Number 2 (18 cubic centimetres)—10 minutes; Number 3 (25 cubic centimetres)—15 minutes.

is, by direct estimations of the total bases. In Tables I to V it is seen that close agreement exists between the neutral chloride found in these two ways. Of course, this agreement would be expected, but only when the nature of the basic radicles of the neutral chloride was comprehensively known. It is therefore proper to conclude that the total bases of the neutral chloride are sodium, potassium,

TABLE V.

Analysis of Series of Specimens from Subject V.

(The results are stated in milliequivalents per litre.)

Substance.	Specimen Number.						
	1	2	3	4	5	6	7
Sodium	33·70	42·20	43·40	24·70	15·50	22·60	30·10
Potassium	14·07	14·75	15·93	18·60	17·23	15·14	14·55
Calcium	3·14	3·08	3·01	2·03	2·95	2·10	3·01
Magnesium	1·03	0·90	1·35	1·42	3·03	1·91	2·37
Ammonium	9·90	11·54	10·00	8·68	7·42	9·88	10·34
Total base	61·84	72·47	74·29	55·43	46·13	51·58	60·37
Total chloride	94·0	94·8	101·0	124·8	125·5	129·3	111·0
Phosphate	3·71	3·71	4·03	2·0	1·76	1·83	2·05
Sum of total chloride and phosphate	97·71	98·51	105·03	126·8	127·26	131·13	113·05
Acid	33·67	23·80	32·67	72·3	81·20	76·70	50·50
Neutral chloride	64·04	74·71	72·36	54·5	46·06	54·43	62·55

All specimens were collected during 15-minute periods. Histamine (0·5 milligramme) was injected at the end of collection of specimen Number 2.

calcium, magnesium and ammonium. Bases other than these are not found. These are present in quantities sufficient in all cases to account for the neutral chloride found by the alternative method of difference between total anion and acid.

A further fact is inherent in these conclusions. In the previous paper it was mentioned that unanimity concerning the proper end-point for acidity titrations in gastric juice does not exist. Not only are different indicators used, but titrations are made of both "free hydrochloric acid" and "total acidity". The values for acidity given in Tables I to V were obtained, as previously stated, by titration approximately to pH 4·3 with methyl orange. This estimation of the acidity gives such a result that it leads, by difference, to a value of the neutral chloride agreeing with the neutral chloride value determined by direct estimation of the total bases. Therefore it is to be concluded that such a procedure gives a true measure of the quantity of hydrochloric acid present in a specimen of gastric juice. This is supported by the author's observation in the previous paper[19] that titration to pH 4·3 with methyl orange indicator gives an accurate estimation of a known quantity of acid in which has been suspended a preparation of gastric mucoprotein.

Reduction of the acidity of gastric juice by the formation of neutral chloride from hydrochloric acid and the protein of mucus has been stated to occur. McCann[13] considers that "the constant association of mucus secreted by the stomach with changes in the acid and chlorides" is evidence of a "protein-acid combining phenomenon" in which the protein of mucus combines with acid to give "an acid mucin and a neutral (base) chloride". Since no modern work on the acid-base binding property of mucoproteins has been done (see Levene[12]), a statement such as that of McCann must be regarded as a quantitatively unsupported hypothesis. Further, the investigation of the quantity and nature of the neutral chloride of gastric juice which is reported in this paper gives no indication that mucoprotein, in the quantities in which it normally occurs (see Table VI) plays any appreciable part in the formation or constitution of the neutral chloride.

TABLE VI.

Averaged Values of Acidity compared with Averaged Values of Protein Nitrogen in Parallel Series of Specimens.

Specimen Number.	Hydrochloric Acid. Grammes *per centum.*	Protein Nitrogen. Milligrammes *per centum.*
1	0·070	75
2	0·057	86
3	0·272	75
4	0·442	27
5	0·459	21
6	0·398	31

Histamine was injected at the end of collection of the second specimens.

Nature of Gastric Juice.

In the present work it has already been indicated that the term "gastric juice" is taken to mean the secretion of the whole stomach. Emphasis upon the products of one kind of gastric gland whilst the products of another kind are not considered must be avoided. From the point of view here adopted the products of the secreting cells may be considered in two classes—those which contain hydrochloric acid and those which do not. These may conveniently be spoken of as the "parietal secretion" and the "mucous secretion" merely as a convenient means of distinguishing them briefly. Therefore, "gastric juice" will be considered to be made up of parietal secretion mixed with mucous secretion. Essentially, these definitions are those which Hollander[10] has found desirable to adopt in order to enable his conceptions to be clearly stated. It has been observed that when the acidity of the gastric juice is greatest and the secretory rate is high, the amount of visible mucus which may be centrifuged from a specimen of gastric juice is very small; with lower acidity and slower secretory rate the proportion of mucus greatly increases. The results in Table VI afford a quantitative illustration of similar findings with dissolved protein. Fuller discussion of the relationship of mucous secretion and mucus itself is entered into below. The secretion of mucus is regarded as a continuous process and not, as earlier investigators have considered, as a secretion which has virtually ceased when acid secretion commences.

The Regulation of Gastric Acidity.

It has been shown by the author in Part I of this paper[19] that mucous secretion contains a sufficient amount of bicarbonate to neutralize considerable amounts of acid. The limiting factors to the extent of this neutralisation, when acid is present in excess, are the total available quantity of mucous secretion and its bicarbonate content. Calculated on the highest value which was found in the estimation reported, 100 cubic centimetres of this mucous

secretion would be able to neutralize approximately 0·056 gramme of hydrochloric acid. The neutralization which occurs involves the irreversible transformation of hydrochloric acid into chlorides of the bases which, as has already been seen, make up the neutral chloride. The neutralization resulting from the mixing of mucous secretion with parietal secretion is a true neutralization of acid. When the formation of a protein-hydrochloride as a means of neutralization of acid by mucous secretion is suggested as a possibility, it is obvious, as Hollander and Cowgill[11] have pointed out, that confusion has occurred between the entire mucous secretion and one of its constituents, mucoprotein. As they rightly conclude, the variations in acidity here being considered result from an irreversible reaction between bicarbonate and acid.

This intragastric mechanism for the neutralization of acid will be a source of neutral chloride in the gastric juice. In addition, the mucous secretion itself contains neutral chloride (see Table IX, also Bolton and Goodhart[4]). It now becomes of interest to examine whether these two sources of neutral chloride are sufficient to account for all the neutral chloride found in the gastric juice after stimulation of secretion with histamine. The total base of anacid specimens is usually greater than the neutral chloride because part of it may be present as bicarbonate. This is particularly striking in the secretion of stomachs showing a true achlorhydria, although it may be inappreciable in the mucous secretion collected from a stomach which has the ability to secrete acid. Hollander[10] states that the total base of the mucous secretion is the source of all the total base (which is equivalent to the neutral chloride) of acid gastric juice. In order to examine this hypothesis of the source of neutral chloride it will be more direct to calculate upon the quantities of total base rather than the anions chloride and bicarbonate. Three methods of calculation will be applied to the results in Tables I and II, in each of which series of specimens a specimen of mucous secretion was obtained before stimulation of the stomach with histamine.

The first method of calculation: An example will be made of the calculation for the second specimen collected (the first after the injection of histamine) from subject I (Table I).

The first specimen (anacid-mucous secretion) was 15 cubic centimetres collected in 30 minutes and containing 73·16 milliequivalents per litre of total base. Therefore, in 15 minutes 7·5 cubic centimetres would be secreted and would contain $\left(\frac{7·5}{1000} \times 73·16\right) = 0·55$ milliequivalent of total base approximately. Now for this calculation let it be taken that the mucous secretion continues at constant rate and is of constant composition. Then of the 13 cubic centimetres collected in 15 minutes for specimen 2, 7·5 cubic centimetres were mucous secretion which contained 0·55 milliequivalent of total base. Therefore 13 cubic centimetres contain 0·55 milliequivalent of total base. This represents a concentration of total base 42·3 milliequivalents per litre. But this specimen was found to contain total base in concentration 71·7 milliequivalents per litre.

Similar calculations have been made for all the other specimens of subject I, of which the analysis is shown in Table I. Also the same procedure has been followed for the specimens of subject II (Table II). In Table VII are shown the results of these calculations compared with the actual quantities of total base found by analysis. In specimen number

Table VII.

Comparison of the Quantities of Total Base calculated by the "First Method" (see text) with those found by Analysis.

Specimen Number.	Volume of Gastric Juice Cubic Centimetres.	Total Base Calculated Milliequivalents per Litre.	Total Base Found Milliequivalents per Litre.
Subject I—			
2	13	42	72
3	38	14	55
4	33	17	40
5	15	37	49
6	7	—	66
Subject II—			
2	13	43	57
3	24	23	41
4	48	12	28
5	16	35	28
6	12	47	60

six in the first series the calculation could not be applied, since only 7·0 cubic centimetres were collected for this specimen. In number five in the second series the total base by calculation exceeded that found by analysis. Therefore, for this specimen, the mucous secretion contains more than sufficient total base to account for the total base found in the gastric juice. In all the other specimens considered, however, it is seen that by this method of calculation there is insufficient total base made available by the mucous secretion to account for the total base of the gastric juice. Before further discussion of the points raised in these calculations, it will be convenient to consider another method of calculation.

The second method of calculation: Hollander[10] states that the secretion of the parietal cells is a solution of hydrochloric containing no fixed base and of a mean hydrochloric acid content of 167 milliequivalents per litre. If the hydrochloric acid is always secreted at this concentration, as Hollander asserts, it will be possible to calculate from the acidity of a given specimen the proportion of parietal secretion which it contains. The remainder of the specimen will then be mucous secretion. The following is an example of the calculation.

In Table I the first specimen (anacid-mucous secretion) was 15 cubic centimetres, collected in 30 minutes and containing 73·16 milliequivalents per litre of total base, which equals 1·1 milliequivalents of total base. The second specimen was 13 cubic centimetres and contained 6·94 milliequivalents per litre of hydrochloric acid, which equals 0·09 milliequivalent hydrochloric acid. This quantity of hydrochloric acid would, according to Hollander, be secreted in $\left(\frac{0·09}{167} \times 1,000\right) = 0·54$ cubic centimetre of parietal secretion. Therefore there were $(13 - 0·5) = 12·5$

cubic centimetres of mucous secretion. This contains $\left(\frac{12{\cdot}5}{15} \times 1{\cdot}1\right)$ = 0·92 milliequivalent total base, assuming that the total base of the mucous secretion remains constant. Therefore the total base $\left(\frac{1000}{13} \times 0{\cdot}92\right)$ = 70 milliequivalents per litre. Actually in this specimen were found approximately 72 milliequivalents per litre of total base.

Similar calculations were made for the other specimens from subject I (Table I) and also for the specimens from subject II. (Table II). The results are shown in Table VIII in comparison with the results found by analysis.

Table VIII.

Comparison of the Quantities of Total Base calculated by the "Second Method" (see text) with those found by Analysis.

Specimen Number.	Volume of Gastric Juice Cubic Centimetres.	Calculated Volume of Mucous Secretion Cubic Centimetres.	Total Base Calculated Milli-equivalents per litre.	Total Base Found Milli-equivalents per litre.
Subject I—				
2	13	12	70	72
3	38	26	51	55
4	33	19	43	40
5	15	10	47	49
6	7	6	64	66
Subject II—				
2	13	9	47	57
3	24	10	28	41
4	48	16	24	28
5	16	6	27	28
6	12	10	61	60

In this Table VIII it is seen that the results obtained by calculation and by analysis agree well in many instances. The essential difference between the two methods of calculation is that in the first method the volume and composition of the mucous secretion are assumed constant, whilst in the second method only the composition is assumed constant. Now in the second method, although the calculated and analytical values for total base usually agree well, the method of calculation is open to the objection that the volume of mucous secretion mixed with parietal secretion to make up the gastric juice would be large in highly acid specimens. These specimens, however, were observed on collection to be non-viscous, watery fluids containing almost no flakes or clots of solid mucus at all. In order to avoid being led into unjustifiable assumptions concerning the nature of what we have termed the mucous secretion, it is necessary to consider whether the products of all the non-acid-secreting cells could under the conditions of these experiments be a fluid containing only little mucus, and, as such, supply the large volumes of so-called mucous secretion which this calculation demands. For, although the term mucous secretion has been used to name this mixed secretion, constancy of its mucus content is not essentially implied in the definition of the term.

The cells which contribute to the mucous secretion are: (i) the mucus-secreting epithelial cells covering the whole gastric mucous membrane; (ii) the mucus-secreting cells of the glands of the cardia; (iii) the principal (pepsin-secreting) cells. The quantity of mucus in the mixed secretions of these types of cells will be large, because mucus-secreting cells probably contribute largely to its composition under normal conditions. This view that the mucous secretion is characterized by the large quantity of mucus it contains is supported by Hollander[9][10] and is implied by Bolton and Goodhart.[5] There is, however, the other alternative to consider, namely, that what we have termed the mucous secretion may sometimes contain very little mucus. Now a return to a conception of a non-mucoid diluting or neutralizing secretion mixed in such quantities as are shown in Table VIII with the parietal secretion cannot be considered. There is no positive evidence for such a conception and there are many opinions against it (Bolderef,[3] Webster,[21] Bolton and Goodhart[5]). The pepsin-secreting cells would be the only possible source of this secretion, but there is no evidence that their secretion is stimulated by histamine. It therefore appears that if the mucous secretion were produced in the increased amounts demanded by the calculations of Table VIII, either much mucus would be present or a diluting secretion would be produced by the pepsin-secreting cells. Since it is impossible to support either of these alternatives, it can only be concluded that such volumes of mucous secretion could not have been added to the parietal secretion. This conclusion is in agreement with the opinions of other workers. For example, Vineberg and Babkin[20] state that histamine activates the cytological elements of the gastric glands which secrete water, hydrochloric acid and other inorganic substances without affecting the secretion of organic substances. Gilman and Cowgill[6] found that histamine did not stimulate pepsin secretion. McCann[13] found evidence that histamine stimulated the secretion of a watery acid solution in place of the mucoid secretion of the unstimulated stomach. Hollander[10] obtained a solution of hydrochloric acid isotonic with the blood and containing no fixed base and therefore no mucous secretion after the injection of histamine. Finally, the results in Table VI of this paper show that the quantity of mucoprotein in solution in gastric juice is greatly reduced as the acidity rises. All these observations support the statement that histamine has no stimulating action upon the quantity of mucous secretion. Therefore it could not lead, as the second method of calculation would demand, to the secretion of sufficient quantities of mucous secretion (of constant composition) to supply the total base found. The first method of calculation also failed to indicate the mucous secretion as the source of sufficient total base to provide all that found in the gastric juice. That is to say, considering both methods, the assumptions that the mucous secretion is in a constant or in a variable proportion of the gastric juice both fail to account for the total base of the gastric juice, provided that

the constant composition of the mucous secretion is assumed.

It remains to consider possible changes of composition. The neutral chloride content of several specimens of mucous secretion collected by the usual gastric and duodenal intubation technique is shown in Table IX. Any variations in successive specimens from the same subject are not great and the variations from subject to subject are also not excessive. These values are similar to those found by Bolton and Goodhart[4] for cats, if exception be made of the high values (0·4% to 0·5%) which they obtained when mucous secretion was "excessively stimulated" by pilocarpine. Since, as has been shown above, the rate of mucous secretion does not rise above the basal level (that existing before histamine stimulation) it will be possible to calculate for the specimens from subjects I and II what total base the mucous secretion would contain if it supplied all the total base of the acid specimens of gastric juice. The values so found by this third method of calculation may be compared with the neutral chloride values of mucous secretion in Table IX.

TABLE IX.

The Neutral Chloride found in Mucous Secretion.

Subject.	Specimen Number.	Neutral Chloride.	
		Gramme Chloride *per centum.*	Milliequivalents per litre.
A	1	0·241	68
	2	0·266	75
B	1	0·254	71
	2	0·253	71
C	1	0·307	87
	2	0·352	99
I	1	0·231	65
II	1	0·235	66

The third method of calculation: Considering the specimen number 2 from subject I, the 13 cubic centimetres collected contained 71·7 milliequivalents per litre of total base, that is, $\left(\frac{13}{1000} \times 71{\cdot}7\right) = 0{\cdot}93$ milliequivalent. If this were derived from the mucous secretion at the basal rate for this subject's test of 7·5 cubic centimetres per 15 minutes, the mucous secretion would contain $\left(0{\cdot}93 \times \frac{1000}{7{\cdot}5}\right)$ = 124 milliequivalents per litre. This equals 0·44 gramme of chloride *per centum.*

Similar calculations for the other specimens from subject I and for the specimens from subject II have been collected in Table X. This table shows that large and irregular variations in the total base of the mucous secretion would occur if all the total base of the gastric juice were derived from this source. In one instance the mucous secretion would need to contain approximately 1% of chloride in order to fulfil the conditions. This result is obviously impossible. In addition, when the irregular variations of the total base in the series of specimens is also considered, it becomes clear that changes in the total base of the mucous secretion cannot be such as will support the hypothesis that the total base of gastric juice is derived from the mucous secretion.

TABLE X.

Calculations of the Amount of Total Base which would be necessary in the Mucous Secretion to supply the Total Base found by Analysis in the Gastric Juice ("Third Method" of Calculation).

Specimen Number.	Subject I. Calculated Total Base expressed in—		Subject II. Calculated Total Base expressed in—	
	Milli-equivalents per litre.	Gramme of Chloride *per centum.*	Milli-equivalents per litre.	Gramme of Chloride *per centum.*
2	124	0·44	92	0·33
3	279	0·99	124	0·44
4	178	0·63	166	0·59
5	97	0·34	56	0·20
6	62	0·22	89	0·32

In recapitulating the conclusions reached this far in the discussion, the following facts may be stated. The mucous secretion is not produced at greater rate after the injection of histamine than before. Calculations based upon Hollander's hypothesis, that parietal secretion is produced at a constant concentration of 167 milliequivalents of hydrochloric acid per litre, lead to the conclusion that large increases in the rate of mucous secretion would occur. Therefore Hollander's hypothesis must be rejected. Constancy of composition of the mucous secretion being assumed, calculations of the total base provided by the mucous secretion proceeding at the basal rate for the test upon the given subject show that a large proportion of the total base found in the gastric juice must be derived from a source other than the mucous secretion. Finally, calculations of the necessary total base of the mucous secretion proceeding at the basal rate for the test upon the given subject demand a total base so variable as to be very improbable or so high as to be impossible. The only possible conclusion to be drawn from these arguments is that the parietal secretion contains total base, that is, that it consists of both hydrochloric acid and neutral chloride. That this represents the nature of the products of the parietal cells is the conclusion of many other investigators (Rosemann,[17] Bolton and Goodhart,[4] Webster,[21] MacLean and Griffiths[14]). Although such a conclusion is the result of the experimental work reported in this paper, as well as that of other investigators, it is nevertheless of value to consider carefully the work which led to the conclusion that hydrochloric acid is secreted at constant concentration. This hypothesis received its most careful experimental support by the work of Hollander.[8][9][10] Now in his last paper[10] Hollander shows that many values for acidity of gastric juice were found besides those of 160 to 170 milliequivalents of hydrochloric acid per litre. A number of them, in fact, were similar to those here reported and from which conclusions opposing

Hollander's have been drawn. It appears that Hollander's highest values do indeed represent the maximal activity of the parietal cells and therefore the greatest possible acidity of the parietal secretion. His lower values show the submaximal secretory activity of the parietal cells. These lower values are of the same order of magnitude as those of the author, which were obtained by submaximal stimulation of secretion by the small dose of only 0·5 milligramme of histamine. It is concluded, therefore, that although the oxyntic glands are shown by Hollander to be capable of producing a solution of hydrochloric acid isotonic with the blood, they normally secrete a fluid in which chloride is present partly as hydrochloric acid and partly in combination with fixed base. In what relative proportions hydrochloric acid and neutral chloride will be found depends upon the secretory activity being manifested at that time by the parietal cells. In the introduction to this paper it was seen that Rosemann arrived at a similar conclusion—that the partition of chloride between hydrochloric acid and neutral chloride depended upon the secretory energy of the [parietal] cells.

The Total Chloride of Gastric Juice.

Rosemann[17] first stated of the gastric juice that what is nearly constant is not the acid, but the total chloride. His conclusions were based upon numerous experiments which, however, were made upon only one dog. Since then it has repeatedly been stated that the total chloride of the secretion of the oxyntic glands is constantly present in quantity of 150 to 170 milliequivalents per litre (or 0·53% to 0·60%). This strength of chloride solution is approximately isotonic with the blood (see, for example, the result of MacLean, Griffiths and Williams,[15] Bolton and Goodhart,[4] Hollander,[10] Gilman and Cowgill[7]). In the tests reported in this paper, forty-two specimens of gastric juice stimulated by histamine were collected from twelve subjects. Omitting the twelve specimens which were collected in the first quarter-hour after the injection of histamine and three specimens that were collected in the fifth quarter-hour, the remaining twenty-seven specimens contained total chloride as follows:—

Total chloride 150 to 161 milliequivalents per litre, 9 specimens.

Total chloride 140 to 149 milliequivalents per litre, 4 specimens.

Total chloride 106 to 139 milliequivalents per litre, 14 specimens.

The total chloride of the gastric juice is seen to approach such a concentration of chloride as is isotonic with the blood. There are, however, many specimens of gastric juice collected during stimulation of secretion by histamine which contain very considerably lower quantities of total chloride than the concentration isotonic with the blood. The effect of mucous secretion mixing with parietal secretion to bring about this state of affairs must be recognized. Since mucous secretion has a lower total chloride than parietal secretion, as has been shown above, the mixing of these two fluids in gastric juice leads to a lower total chloride in the mixture than occurred in the parietal secretion. As long as appreciable quantities of each of these secretions are mixing in variable proportions, the total chloride of the gastric juice will be variable. It is possible, however, that the variations in the total chloride of the gastric juice may not all be attributed to this cause. Whether a concentration of chloride isotonic with the blood constantly represents the level at which this radicle is always secreted by the oxyntic glands is not certain. Whilst no doubt exists that the level of the blood electrolytes is a controlling factor of the total chloride, which is never secreted in solution hypertonic to the blood (Gilman and Cowgill[7]), it may be that the total chloride is hypotonic to the blood at times when the stimulation to secretion is slight or submaximal. Such methods of calculation as were used in the discussion of constancy of acidity do not lead to unequivocal results when applied to the total chloride in a series of specimens from one subject.

It is noteworthy that MacLean and Griffiths[14] concluded that "the gastric secretion under normal conditions has approximately the same concentration of Cl. equal in strength to about 0·11 normal." This conclusion was based upon the results of test-meals containing sodium sulphate. The results of the author[18] using two test-meals, one of gruel and one of cream, on the same subject showed that the concentration of total chloride reached a value of approximately 0·11 normal. In the same subject the total chloride reached approximately the same constant value with each kind of meal. That the curve for the total chloride with two kinds of test-meal upon the same subject rises in each case to the same level of 0·10 to 0·12 normal (100 to 120 milliequivalents per litre) throws little light upon the total chloride concentration of the parietal secretion. There is unequivocal evidence that the total chloride of gastric juice is variable and that the total chloride of the parietal secretion may reach, as a maximum (Gilman and Cowgill[7]), a concentration isotonic with the blood. The further conclusion that the total chloride of the parietal secretion is always of the constant value isotonic with the blood under all conditions goes a stage further than the experimental evidence of the present inquiry can confirm.

Summary.

1. The nature of the neutral chloride of gastric juice has been determined.

2. The relationship of the hydrochloric acid content of gastric juice to the total and neutral chloride has been investigated.

3. By calculations upon the quantity of total base in mucous secretion and in whole gastric juice of

the same subject, it has been shown that total base (that is, neutral chloride) must be secreted along with hydrochloric acid. It is concluded that hydrochloric acid is secreted in variable concentration by the parietal cells, and the proportion of total chloride secreted as hydrochloric acid at a given time depends upon the secretory activity of the parietal cells.

4. Hydrochloric acid cannot be secreted in concentration greater than that of a solution of hydrochloric acid isotonic with the blood.

5. Similarly, the concentration of total chloride in the secretion of the parietal cells is limited in the same way. Whether this limiting concentration of total chloride represents the level at which it is always secreted is considered uncertain.

6. The total chloride of gastric juice is made up of the chloride of the parietal secretion and the mucous secretion in variable proportions, and is therefore a variable.

Acknowledgement.

The author most gratefully acknowledges his debt to Associate-Professor Henry Priestley, whose critical discussions of the experimental results are responsible for the presentation of this paper in its present form.

References.

(1) W. Boldereff: *Pflüger's Archiv für die Gesammte Physiologie*, Volume CXXI, 1907, page 13.
(2) W. Boldereff: *The Quarterly Journal of Experimental Physiology*, Volume VIII, 1914, page 1.
(3) W. Boldereff: *Bulletin of the Battle Creek Sanitarium*, Volume XXIV, 1929, page 379.
(4) C. Bolton and G. W. Goodhart: *The Journal of Physiology*, Volume LXXIII, 1931, page 116.
(5) C. Bolton and G. W. Goodhart: *The Journal of Physiology*, Volume LXXVII, 1933, page 287.
(6) A. Gilman and G. R. Cowgill: *The American Journal of Physiology*, Volume XCVII, 1931, page 134.
(7) A. Gilman and G. R. Cowgill: *The American Journal of Physiology*, Volume CIII, 1933, page 143.
(8) F. Hollander: *The Journal of Biological Chemistry*, Volume LXXIV, 1927, Proceedings page 23.
(9) F. Hollander: *The American Journal of Physiology*, Volume XCVIII, 1931, page 551.
(10) F. Hollander: *The Journal of Biological Chemistry*, Volume XCVII, 1932, page 585.
(11) F. Hollander and G. R. Cowgill: *The Journal of Biological Chemistry*, Volume XCI, 1931, page 151.
(12) P. A. Levene: *"Hexosamines and Mucoproteins"*, 1925, page 124.
(13) J. C. McCann: *The American Journal of Physiology*, Volume LXXXIX, 1929, page 483.
(14) H. MacLean and W. J. Griffiths: *The Journal of Physiology*, Volume LXV, 1928, page 63.
(15) H. MacLean, W. J. Griffiths and B. W. Williams: *The Journal of Physiology*, Volume LXV, 1928, page 77.
(16) J. P. Pavlov: "The Work of the Digestive Glands", Translated by W. H. Thompson, 1910.
(17) R. Roseman: *Pflüger's Archiv für die Gesammte Physiologie*, Volume CXVIII, 1907, page 467.
(18) G. V. Rudd: *The British Journal of Experimental Pathology*, Volume XI, 1930, page 240.
(19) G. V. Rudd: "Studies on the Composition of Gastric Juice", Part I, The Medical Journal of Australia, March 31, 1934.
(20) A. M. Vineberg and B. P. Babkin: *The American Journal of Physiology*, Volume XCVII, 1931, page 89.
(21) D. R. Webster: *The American Journal of Physiology*, Volume XC, 1929, page 718.

OBSERVATIONS ON HÆMOCHROMATOSIS.

By Kempson Maddox, M.D. (Sydney), M.R.C.P. (London),

Honorary Assistant Physician and Medical Officer to Diabetic Clinic, Royal Prince Alfred Hospital, Sydney;

AND

E. Beatrix Dubie, B.Sc., M.B., Ch.M. (Sydney),

Biochemist to Royal Prince Alfred Hospital and Diabetic Clinic, Sydney.

(From the Diabetic Clinic, Royal Prince Alfred Hospital, Sydney, Australia.)

First described by Troisier in 1871 and named "hæmochromatosis" by von Recklinghausen in 1889, this disorder has received attention out of all proportion to its frequency or importance. This is undoubtedly due, in part, to its widespread and outspoken clinical features, and in part to the obscure nature of its origin. By 1932, 175 cases had been reported (Stetson and Ferris[1]). Three more have appeared in American literature since. It is doubtful whether this figure includes Australian cases, of which six have been recorded (Grieves,[2] Stokes,[3] Russell,[4] McWhae[5]). The disease is, however, commoner than these statistics indicate. Our attention was directed to the subject by the simultaneous appearance in the same medical ward of three male patients suffering from the condition.

Case Histories.

Brief clinical histories of these patients, and of one additional female patient, follow. The chief clinical and biochemical findings are shown in tables, and are omitted from the text.

Case I. W.T., aged thirty-three years, a bank teller, was admitted to hospital on February 1, 1932. He stated that he had felt well and active up to fourteen months previously, when he began to suffer from attacks of *pruritus ani* and furunculosis, vomiting and drowsiness. Frequency of micturition and polyuria for two months before admission were accompanied by increasing thirst and hunger. He lost 23 kilograms of weight during this period; the loss of weight was accompanied by increasing lassitude and nocturnal cramps in the lower limbs. He said that his face was very sunburned, but thought that the colour had turned to a deeper hue during the preceding two years. Examination showed him to be wasted and of a dusky slatish hue, apparent all over the body, but with darker patches over the dorsum of the neck, hands and forearms. The liver was firm, smooth and hard, extending four fingers' breadth below the costal margin. No enlargement of the spleen was present. Urine on his admission contained albumin 1%, abundant sugar and ketones, with some hyaline and granular casts.

Section of the skin from the upper arm showed granules, stained by the Perl method, around the sweat glands and between them and the superficial epithelium. He received at first a daily diet of 1,330 calories (fatty acid : glucose ratio, unity), and 90 units of insulin, given in three equally divided doses. This failed to control the glycosuria, yet he suffered from several severe attacks clinically resembling hypoglycæmia. It was then discovered that he had a lowered renal threshold, and the insulin was reduced to 75 units daily. The insulin was given in doses of 45, 15 and 15 units, but his severest insulin attack

followed, only relieved with difficulty by sugar by the mouth. He was unconscious for nearly an hour. Observations of the blood sugar were now used as controls in preference to observations on the urinary sugar, but attacks still occurred at irregular intervals, even though for a time the diet and insulin received were kept constant. After the findings recorded in Chart I, his insulin was suspended for a week without any difference occurring in his weight or amount of urinary sugar, though he complained of a return of the skin irritation and polyuria. The insulin was resumed at 40 units daily with a diet of 1,650 calories.

He gained three kilograms in weight while in hospital, and after his discharge, attended the Diabetic Clinic for three months. At each visit his urine, especially the early morning specimen, was found to contain abundant sugar, but no acetone. Acetone was rarely present at any stage. A further attack of boils and a subcutaneous abscess were associated with an increase in urinary sugar, but not in ketones.

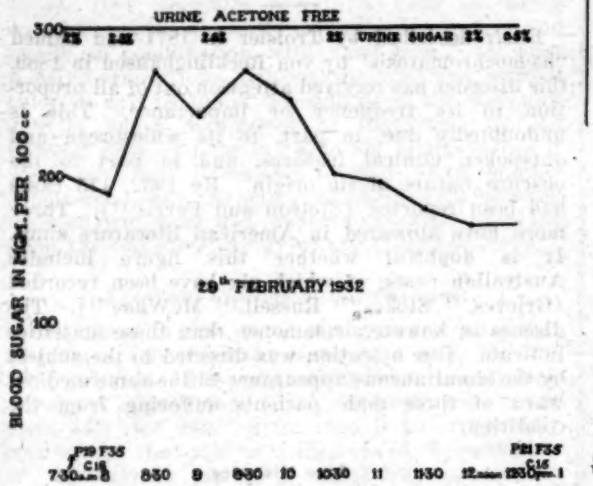

Chart I.

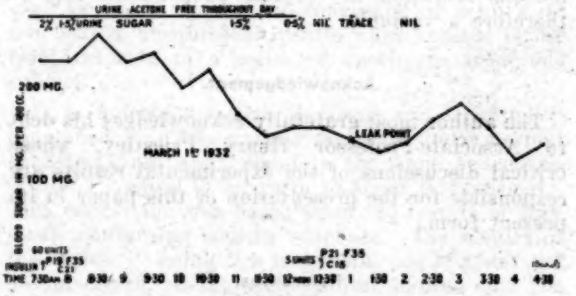

Chart II.

Charts I and II show half-hourly estimations of the capillary blood sugar in Case I on two successive days. No insulin was given on February 29 (Chart I); the administration of insulin on March 1 is indicated by arrows. The nature and quantity of food are represented by the letters P = protein, F = fat, and C = carbohydrate, followed by figures indicating the number of grammes of each food given. It will be observed that the blood sugar curve was apparently very little affected by the insulin. The blood sugar was estimated by the method of Hagedorn and Jensen.

Communicated with a year later, he stated that he felt very well and was able to do eight consecutive hours' gardening once a week; that his weight had increased by 2·1 kilograms (five pounds), and that his colour had "improved wonderfully". His glycosuria is less, sometimes being present in the late afternoon, with a complete absence of acetone from the urine, while he is taking 15 units of insulin twice daily. Typical hypoglycæmic attacks, relieved by barley-sugar, had occurred about midnight for several months, and meanwhile he had developed rheumatoid arthritis in his fingers and knees.

Case II. J.K., aged fifty-nine years, a retired post office clerk, was first admitted to hospital for two months in 1925, complaining of the symptoms of *diabetes mellitus*. He passed only small amounts of sugar and few ketones on a daily diet of 2,200 calories, with 30 units of insulin daily. His fasting blood sugar was never raised above 190 milligrammes *per centum*. No note was made of pigmentation nor of any enlargement of the liver.

He continued attending as an out-patient, on a diet of approximately 1,500 calories and 18 units of insulin daily. His fasting blood sugar during this period averaged 180 milligrammes *per centum*, and no ketones were passed, while his weight remained constant. He was readmitted in January, 1929, following an attack of diarrhœa, and was diagnosed by Professor A. E. Mills as suffering from hæmochromatosis, as his liver was palpable 7·5 centimetres (three inches) below the rib margin, and the spleen was said to be enlarged. His condition was controlled by a diet of 2,200 calories with five units of insulin twice daily. During the next three years a gradual rise occurred in the fasting level of the blood sugar, necessitating an increase in his insulin to 20 units daily. He was a difficult patient to control, and raised his diet and insulin at his own will. He entered hospital for the last time at our request on February 12, 1932. He admitted that his colour had become darker during the past two years. His chief complaint was severe epigastric pain of ten weeks' duration. He stated that he had experienced many insulin reactions on unexpected occasions.

His colour was the darkest in the series; it was of a striking slate-blue hue. Pigment was most heavily marked in dark patches on the shins and on the outer aspect of the forearms and hands. The liver was hard, smooth and enlarged to the umbilicus with a large boss on the anterior surface. The spleen was palpable. His hyperglycæmia was controlled by a diet of 1,520 calories and 30 units of insulin, during which period no insulin attacks occurred and the investigations recorded in the tables were undertaken.

He attended the Diabetic Clinic at monthly intervals, becoming progressively weaker and complaining of increasing epigastric pain for six months. The urine at this time was frequently sugar and acetone free.

He died at home on November 18, 1932. No autopsy was possible.

Case III. M.R., a female, aged forty-three years, a barmaid, was known to have had glycosuria for three years. She was first admitted to hospital on January 5, 1930, complaining of weakness, tiredness and shortness of breath. She had been previously troubled by severe pains in both arms and by cramps in the lower extremities.

On examination the liver was 7·5 centimetres (three inches) below the costal margin; it was hard and smooth, and the spleen was palpable. Her heart at this time was said to be normal and no other abnormality was recorded. Fifteen months later she was readmitted complaining of great nocturnal pain in the left arm. The liver was stated to be 10·0 centimetres (four inches) below its normal level and the spleen was still readily felt. She stated that she had also suffered from frequent boils meanwhile and her fasting sugar varied between 280 and 411 milligrammes *per centum*.

Examination of skin at this time revealed appearances typical of hæmochromatosis. Five months later she was admitted again, on this occasion she was short of breath and had swollen abdomen and legs. Her heart was said to be enlarged and the sounds were very weak. She made a slow recovery and was able to be discharged in a walking condition with a pulse rate about 100 to the minute.

TABLE I.

Observation.	Case I.	Case II.	Case III.	Case IV.
Blood pressure, in millimetres of mercury	120/80	125/75	95/60	90/70
Arterial thickening	Nil	Definite	Slight	Slight
Electrocardiogram	*T* waves flat, inverted, Leads II and III	—	—	Elevated *S-T* interval. Low voltage
Blood count—				
Red cells, per c.mm.	4,700,000	4,480,000	3,360,000	4,720,000
White cells, per c.mm.	3,300	4,700	4,500	10,000
Colour index	0·9	1·0	1·1	1·0
Fractional meal	Hydrochlorhydria	Normal	—	Achlorhydria
Bismuth meal	—	Normal	Gastroptosis	Normal
Wassermann test (blood)	No reaction	No reaction	No reaction	No reaction
Basal metabolic rate	± 0	—	—	—
Urea concentration	3% in first hour	—	2·15% in 2 hours	—
Blood urea	34 mgm. %	60 mgm. %	—	—
Blood cholesterol	—	—	135 mgm. %	—
Carbon dioxide combining power of plasma	20 vols. %	48 vols. %	—	—
Urinary diastase	—	—	3·3 units	—
Van den Bergh reaction	Direct and indirect negative	—	—	Indirect, slightly positive
Adrenaline eye test	No reaction	No reaction	No reaction	No reaction
Graham's test	—	Positive	Positive	Positive
Perl reaction (biopsy of skin)	Positive	Positive	Positive	Positive

Her fourth and last admission to hospital was at our instigation for the purpose of closer investigation, on June 9, 1932. Her complaint at this time was merely of lassitude and weakness. She stated that she had had a recurrence of the dropsy in the interim and had suffered a severe hæmorrhage after tooth extraction. She was still affected by swollen ankles at times and claudication in the legs, and had had attacks of diarrhœa accompanied by light coloured stools. As her diabetes had been quite uncontrolled since her previous admission, she was further affected by polydipsia, polyphagia, and polyuria. She complained also of epigastric pain after food or drink. She was placed on a diet of 750 calories, with a fatty acid: glucose ratio of 1·5, which kept her urine sugar free, except for the early morning specimen, which was heavily loaded. No ketones appeared in any specimen. In appearance she was extremely emaciated, weighed only 25 kilograms (four stone), and was of the typical bronze hue. The pigmentation was most heavily marked on the face, neck, forearms, hands and shins. The patient's skin was dry and scaly, and the thyreoid gland impalpable. The liver was uniformly enlarged, smooth, tender and indurated, reaching six fingers' breadth (13·75 centimetres or five and a half inches) below the ribs. Dilated superficial veins coursed vertically upwards over the abdomen. Many small petechiæ were visible on all extremities. The

TABLE II.

Showing Synopsis of Progress in Carbohydrate Tolerance.

Case.	Date.	Diet (Calories).	Daily Insulin (Units).	Fasting Blood Sugar (milligrammes *per centum*).	Urine Sugar.	Urine Ketones.
I.	29/1/32	1,330	90	280	2%	Trace
	4/2/32	1,330	60	241	2%	—
	13/3/32	1,500	35	260	2%	—
	24/4/32	—	35	—	2%	—
II.	1925	2,200	30	190	Trace	Trace
	1926-1929	1,500	18	180	Trace (occasionally)	Trace (occasionally)
	6/1/29	2,200	10	—	—	—
	12/2/32	1,900	—	141	—	—
	26/2/32	1,500	—	222	—	—
	4/3/32	1,500	—	132	—	—
III.	16/1/30	1,200	50	222	Trace	—
	23/1/30	1,000	90	280	—	—
	5/3/31	—	31	411	+	+
	14/3/31	—	—	280	—	—
	24/6/31	1,600	60	290	3·8%	—
	8/8/31	—	—	350	—	—
	9/6/32	—	—	310	3%	—
	1/7/32	2,600	75	177	2%	—
	5/9/32	—	50	97	—	—
IV.	29/1/32	1,000	25	241	3%	—
	4/3/32	—	—	222	Trace	+
	11/3/32	1,200	50	150	Trace	+
	14/4/32	1,200	50	88	—	—
	26/4/32	1,200	—	370	5%	++
	17/5/32	1,200	—	419	3%	++

Note.—No conclusions as to renal threshold may be drawn from the above, as urine in most instances is that first passed in the morning.

patient's ankles were œdematous and the *dorsalis pedis* artery was impalpable, though the radial vessels were but slightly thickened. Her knee jerks were absent, and the heart was generally dilated. During a month in hospital she gained eight kilograms (one and a quarter stone), and was discharged at her own request.

She was now on a diet of 2,600 calories, and was taking 50 units of insulin daily; her urine was mostly sugar free. Two hypoglycæmic attacks occurred unexpectedly while she was at rest in bed in hospital. Seen again three months later, she was paler, weaker, and had abundant glycosuria.

She died shortly afterwards at home. No details were supplied and no *post mortem* examination was possible. The remaining clinical and biochemical findings appear in the tables.

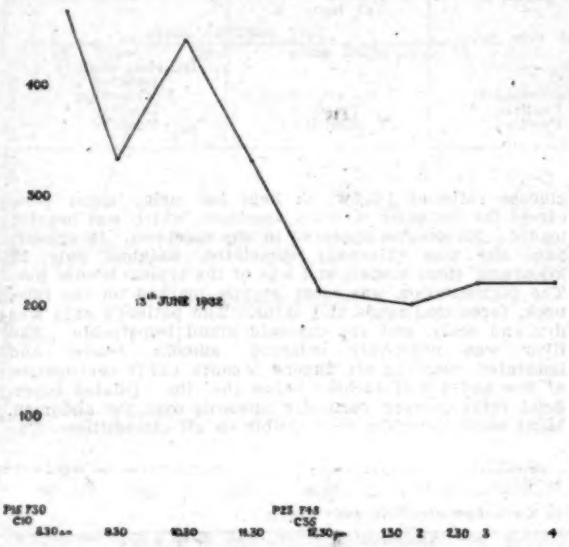

Chart III.

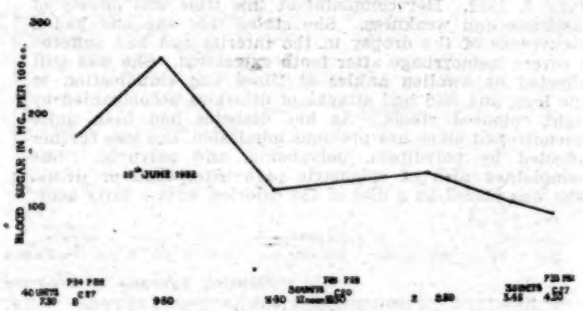

Chart IV.

Charts III and IV show the daily variations of the capillary blood sugar in Case III. The administration of food and insulin is indicated by arrows, as in Charts I and II. The effect of insulin was much more apparent in this case.

Case IV. M.C., aged fifty-six years, a cooper, was admitted to hospital on January 29, 1932. After a period of three months thirst and polyuria, he said he felt "run down due to an unusual amount of worry". Neither he nor his wife thought that he had changed at all in colour, but he had lost 12·7 kilograms (two stone) in weight. He had suddenly become near-sighted and had latterly suffered from severe nocturnal cramps in the legs. In appearance he was very thin, and manifested the dusky hue of the disease, though to a less degree than the other patients. His pigmentation was particularly heavy on the forearms, and over the tibiæ took the form of large irregular patches of dark brown on a skin of a leaden hue. On section of a piece of skin from the arm, free iron was visible round the sweat glands. There was slight œdema of both ankles, and the inguinal glands appeared rather large but discrete. Dilated veins were visible on part of the abdomen. The liver was regularly enlarged and very hard, extending to four fingers' breadth below the costal margin. The remaining systems were unaffected. He remained in hospital eight weeks and has since been in attendance at the Diabetic Clinic. Though passing sugar at intervals, his urine is mainly sugar free on a diet of 1,500 calories of a fatty acid : glucose ratio of 1·5, with 50 daily units of insulin, and there has been no noticeable deterioration in his physical condition or body weight during the past year, and he states that he feels well. Deliberate stoppage of his insulin caused a progressive rise in blood sugar from 88 to 419 milligrammes *per centum* in three weeks, with the appearance of ketones in the urine.

Remarks on Certain Clinical Features.

The classical diagnostic features of the disease do not require enumeration, but we propose to comment on a few common signs from the clinical point of view.

Pigmentation.

The distribution of the skin pigment is generally said to be universal. In each patient of this series it tended to be especially marked on the extensor aspects of the extremities, and around the neck. This corresponds to the additional pigmentation seen in the exposed areas in Addison's disease, and may be due to an added melanosis, from the effects of air and light, rather than from those of pressure and irritation (Rous,[7] Rolleston[8]). The mucous membranes are usually said to be unpigmented and certainly there is no obvious patchy discoloration of the type seen in adrenal failure. Nevertheless in two of our four patients a diffuse slaty-blueish colour was visible in the hard palate, which strongly suggested a similar process to that seen in the skin, but modified by the nature of the epithelium. No examination has been made of the palatal mucous membrane and we did not consider it justifiable to excise a small piece for examination.

A similar discoloration of the retina was observed in three of the patients. The latter phenomenon was quite striking and was associated with an ochre coloured background in the periphery of the fundus.[36]

Examples of hæmochromatosis are said to occur without skin pigmentation (Telling,[12] Stewart, Orr[13]). Some of these patients may develop pigmentation subsequently, though others die unpigmented (Orr[13]). A feature seen in three of the present series was the definite variation in facial hue seen from time to time, noticed also by Donaldson[14] and Hodges.[15] Since consideration of the changes of carbohydrate metabolism shows a varying disability, it is conceivable that if the hepatic function improves for a time, pigment may actually be reabsorbed from the deeper layers of the skin. In two instances (Cases II and III) the facial colour became paler and less noticeable as the patients' condition deteriorated. This was probably

due to a cachectic element manifesting itself even in the pigmented skin. The initial onset of the pigmentation is so insidious and gradual that it is frequently unnoticed by the patient or his friends, and he may deny that it is anything more than his usual summer tan, a local difficulty which does not occur in England.

The Cardio-Vascular System.

There is no evidence here or elsewhere to suggest that the disorder has any relationship, either causative or aggravatory, upon cardio-vascular degeneration, beyond that commonly associated with a prolonged hyperglycæmia. The blood pressure in Case III was depressed, but at a time when the patient was markedly emaciated and bedridden. Œdema of the ankles is frequently recorded, but this is common in cases of hepatomegaly or ascites. Stetson and Peter's patient developed paroxysmal fibrillation following a coronary occlusion. Gross myocardial failure occurred in Case III a few weeks after an attack of precordial pain and dyspnœa following pneumonia. Clinical, radiographic and cardiographic evidence was absent as far as frank circulatory damage was concerned in each of the remainder of the group. No calcification could be seen in a soft radiogram of the tibial vessels of Case I.

The Blood.

Anæmia and increase of bilirubin are significantly absent in all uncomplicated cases. One cell count in Case III showed a mild microcytic anæmia. Eosinophilia up to 5% of the total white cells occurred in Cases II and III. Lawrence[25] and Buckley have observed the same phenomenon in insulin-treated diabetics. Stetson and Ferris[1] assert that purpura or some other hæmorrhagic manifestation occurred in 9% of 153 patients. We agree with Potter and Milne[17] that some such manifestation is no more common than in other types of hepatic cirrhosis. The coagulation and bleeding times in the case described by Stetson and Ferris[1] were normal. Both their patients suffered from scurvy, the development of which on a deficient diet, the authors believe to be enhanced by hæmochromatosis. They hold this belief on the ground that the interference with liver function affects the production of fibrinogen, and that vitamin *C* may be inadequately absorbed through a damaged portal system.

If this be true, it would be expected that more patients would develop spontaneous purpura and scurvy. Two of our patients showed odd petechial spots on the hands, and one (Case III) severe hæmorrhage after tooth extraction.

The Alimentary Tract.

Including the results obtained by the fractional test meal, there are no constant abnormalities of the upper part of the alimentary canal. Radiographic examination was equally uninformative, beyond the demonstration of gall-stones (Case II) and poor filling of the gall-bladder with dye (Case III), probably a sign of hepatic inactivity. We had the impression that a plain radiogram of the liver in Case I was denser than usual. Shattock[18] denies that this occurs.

Mills[21] states that cases may occur showing no hepatic enlargement. This must be rare and probably depends on excessive shrinkage of the fibrous septa. Ninety-five *per centum* of 53 patients collected by Blanton and Healy[19] showed liver enlargement at autopsy, though on purely clinical grounds only 80% were said to be enlarged. Both our patients who died complained bitterly of epigastric pain for some weeks before death. Rosenthal has also recorded this. In so far as it seemed to be aggravated by movement, the pain was thought to be due to perihepatitis, but no evidence of perihepatitis has been noted in accounts of autopsies given in the literature.

Diarrhœa and vomiting were not observed by us beyond a history that it occurred on two occasions in Case III, accompanied by light coloured stools, such as is frequently given by patients with portal obstruction from other causes. Hæmatemesis is notably absent, as is ascites, symptoms which may be related to the denser fibrous and atrophic liver of Laennec's cirrhosis. Both stomach contents and stools were free from occult blood in all four persons under our observation.

Family History and Previous Health.

Hæmochromatosis has not been observed to be familial, nor has any common acute fever been reported as being frequent in the history of patients already recorded. In the present series typhoid fever, influenza, tonsillitis, scarlet fever and pneumonia appear in the record of past illnesses. Gastro-intestinal disturbances were conspicuous by their absence, except until after the establishment of the hepatic cirrhosis. With reference to the family health, however, one feature deserves mention, namely, that *diabetes mellitus* occurred in relatives of three of the four patients. In one instance a brother, in another a sister, and in another a great aunt had died in diabetic coma. In view, however, of the definitely secondary nature of the diabetes in hæmochromatosis, a minimum of importance can be attached to these circumstances in such a small series, though such a diathesis may perhaps determine an earlier and more severe disturbance of carbohydrate metabolism. A family history of carcinoma and the concurrence of syphilis are equally uncommon.

The Influence of Sex and Occupation.

One of the most interesting features of the disease is its almost complete preference for the male sex. Up to 1929 only four cases had been described in women (Donaldson[14]). Another has been recorded since by Hodges. Rolleston has

expressed the sex ratio as follows: cirrhosis, men 2 to 3 times, cancer of the liver 10 times, hæmochromatosis 40 times, commoner in men than in women.

There is one female in our series of four instances of the disease and the features and progress of her case presented no difference from those of the others. No cases have been reported in children (Mills[21]). The reason for this anomaly is unsolved, but the sex distribution follows that of hepatic cirrhosis in general, to explain which the greater frequency of alcoholic drinking in the male has been postulated. The distinction has, however, in regard to hæmochromatosis, been explained by Mallory[30] and others as intimately bound up with the question of occupation and exposure to iron, copper and alcohol. It is worthy of repetition that the woman, Case III, of the series, was a barmaid, and this work has preceded the appearance of hæmochromatosis in patients described by other observers. The remaining patients, however, including our own, were temperate. It is relatively easy to establish in many occupations a close exposure to metals, especially iron. One of our patients was a cooper, another a bank teller, who, apart from handling coins all day, lived for some years previously in the Gulf country of North Australia, where the drinking water was collected from clay pans. Barber's[22] patient worked for thirty-five years in an iron foundry, and half of the patients in Mills's[21] series had worked with copper. On the whole, however, the evidence for metallic occupational sources, as an indispensable causative factor, remains unconvincing.

The Carbohydrate Metabolism.

In the few instances in which the carbohydrate metabolism has received close and continued observation, features have revealed themselves which at once distinguish the disturbance from that commonly encountered in *diabetes mellitus*, and even throw doubt on the wisdom of using the term diabetes.

The first question to discuss is how glycosuria and hyperglycæmia occur at all. In certain instances no glycosuria has been reported (Orr[13]). In others diabetes is said to have been present for some years before the appearance of pigmentation or hepatomegaly, even allowing for the fact that there is no special reason why hæmochromatosis should not complicate a case of pre-existent *diabetes mellitus* (Mills[21]) and that early degrees of hepatic enlargement may be difficult to detect by clinical methods. All our patients followed the general rule by first presenting themselves with the symptoms of hyperglycæmia.

It is generally accepted that the diabetic symptoms show themselves at a period coincident with the spread of the pigmentation of cirrhosis, or both, to the islets of Langerhans. A critical survey of the descriptions of the findings at autopsy available in the literature at our disposal shows that no such correlation can be allowed. In Barber's[22] case no trace of the islets could be found. In many others, however, though the pancreas is cirrhotic to a degree similar to that seen in portal cirrhosis, the islets are less fibrosed and less pigmented than the surrounding acini. They are also free from the hyaline appearance seen after death from *diabetes mellitus*. The external secretion of the gland, nevertheless, seems adequate. It is highly probable that in the majority of patients, the cause of the disturbed carbohydrate metabolism must be sought elsewhere. By this we do not mean to deny a pancreatic factor in the hyperglycæmia, as certain patients are definitely benefited (for example, Case IV) by insulin therapy, but it is not possible on the grounds of a purely pancreatic inadequacy to explain the following anomalies of glucose metabolism observed in hæmochromatosis.

Firstly, these patients display an extraordinary "resistance" to insulin, whereby large doses of reliable insulin, for example, 70 units, cause a minimal fall in the blood sugar (Chart II). This feature has been noted by a number of observers (Root,[41] Stetson and Peters,[16] Critchlow,[23] Allan and Constam[42]). Since the usual action of insulin appears to be the facilitation of rapid removal of sugar from the blood to the hepatic cells, it is to be presumed that either as a result of the initial damage to the liver, which originated the disease, or as a result of the pigmentation therein, the storage capacity of the liver for glycogen has become restricted. Since the pigment clusters in the cells occupy the very situation usually taken by glycogen granules, it is tempting to assume that this is the histological counterpart of this functional disability.

The fact that cases are known in which hyperglycæmia has preceded skin pigmentation by a number of years, does not prove that pigmentation in the liver was not already present. The rarity of the diabetic syndrome in portal cirrhosis must lend support to the theory that the presence of heavy pigmentation in the liver may be the additional factor causing hyperglycæmia in hæmochromatosis.

The origin of *diabetes mellitus* remains obscure, but there is a growing interest in the rôle of hepatic activity in this disease. In this connexion it is of interest to recall a case of hyperglycæmia, due to deficient glycogen storage, in a boy with a purely hepatic cirrhosis, reported by Wagner and Parnas,[24] in which a completely normal pancreas was found at autopsy. From a fasting blood sugar of 80 milligrammes *per centum* his blood sugar after food rose to 420 milligrammes *per centum*. There must, however, be other reasons than liver cirrhosis and pigmentation for insulin inactivity, which are perhaps associated with other endocrine dysfunction, as for example the boy reported by Lawrence,[25] in which both these features were absent. In this article, he concluded tentatively that some enzyme necessary for the conversion of

hexose phosphate to glycogen was missing. Himsworth states that the degree of difference in sugar content between arterial and venous blood depends on the amount of insulin present in the body. His investigation of this index in normal individuals seems to show that insulin, as secreted by the pancreas, is inactive, and a latent period ensues before activation occurs. He states that the duration of this period varies with the capacity of injected insulin to depress the arterial blood sugar. Markowitz,[27] Mann and Bollmann have found that immediately after the removal of the liver, insulin is rapidly effective, but after a few hours it loses its capacity. Himsworth himself observed the development of insulin resistance following thrombosis of the hepatic artery. He concludes that an insulin kinase is produced in the liver. If this is so, the damage and pigmentation sustained by the hepatic cells in hæmochromatosis would seem to be sufficiently generalized and outspoken as to inhibit its formation in whole or in part.

With this work in mind, we administered an ampoule of soluble liver extract, prepared by Parke, Davis and Company for the treatment of macrocytic anæmia to the patient in Case IV, together with glucose and insulin, following a control observation of the effect of the insulin alone on the blood sugar level, as follows:

Sugar Tolerance Test. "A".

50 grammes of glucose and 25 units of insulin given.

	Milligrammes *per centum.*
Blood sugar before glucose	370
Blood sugar ½ hour after glucose	353
Blood sugar 1 hour after glucose	343
Blood sugar 1½ hours after glucose	394
Blood sugar 2 hours after glucose	353

Urine: 5% sugar and +++ Acetone.

Sugar Tolerance Test. "B".

50 grammes of glucose, 25 units of insulin and 2 cubic centimetres liver extract given.

	Milligrammes *per centum.*
Blood sugar before glucose	419
Blood sugar ½ hour after glucose	447
Blood sugar 1 hour after glucose	353
Blood sugar 1½ hours after glucose	353
Blood sugar 2 hours after glucose	343

Urine: 3% sugar and ++ acetone.

The negative result was not unexpected as the insulin kinase, if present, will probably be as difficult to isolate in an active form as insulin itself.

The unsatisfactory results of tests for hepatic efficiency are related to the fact that each test investigates only one of the liver's metabolic activities, and one which may not be depressed in the particular case under trial. Many patients with *diabetes mellitus* show a lævulose intolerance; in Case IV the patient, who was the only one to undergo this test and who seems to be the most benefited by insulin, also showed a rise in blood sugar, as follows:

Lævulose Tolerance Test.

	Milligrammes *per centum.*
Blood sugar before 50 grammes of lævulose	321
Blood sugar ½ hour after 50 grammes lævulose	343
Blood sugar 1 hour after 50 grammes lævulose	411
Blood sugar 1½ hours after 50 grammes lævulose	343
Blood sugar 2 hours after 50 grammes lævulose	251

The absence of an increase in the blood sugar following an injection of epinephrine is said to indicate deficient glycogenlysis on the part of the liver (Lawrence,[25] Cammidge and Poulton[28]), though Corkill[29] has shown a glycogenetic effect in the livers of fasting rabbits. Hypodermic injection of 0·6 mil (ten minims) of epinephrine in Case IV gave the following result:

Epinephrine Test.

	Milligrammes *per centum.*
Blood sugar 9.50 a.m. before epinephrine	280
0·6 mil or 10 minims of epinephrine given.	
Blood sugar at 9.55 a.m.	270
Blood sugar at 10.5 a.m.	241
Blood sugar at 10.30 a.m.	280
Blood sugar at 10.50 a.m.	331

The next anomaly observed in the carbohydrate metabolism of patients with hæmochromatosis is the spontaneous irregular variation which occurs in glucose and insulin tolerance. Spontaneous hypoglycæmia may occur for no obvious reason under constant conditions of glucose and insulin administration. The margin between insulin shock and glycosuria may be very fine, a decrease of five grammes of carbohydrate being sufficient at times to provoke an insulin attack (Stetson and Peters[1]). The same phenomenon was observed by us (Cases I and III). Our difficulties were increased in Case I by the presence of a low renal threshold at 140 milligrammes *per centum* of blood sugar. Depression of the leak point as in Case I did not occur in the remainder of this or other recorded series. The carbohydrate tolerance also varied in a phasic fashion from time to time, which suggests a varying inability of the liver to store glycogen, associated with a failure of the diseased organ to free glucose with sufficient rapidity. Hepatic hypoglycæmia is becoming more recognized (Cammidge and Poulton[28]). It does not seem to occur with Laennec's cirrhosis, and may be dissociated from interference with urea or bile formation. Difficulty was experienced in Case I in relieving the patient, who remained semi-conscious for almost an hour. Stetson and Peters[1] had the same experience, following the giving of orange juice by mouth, whereas glucose injected into the veins was immediately successful. This may be due to a delayed absorption from portal stasis, but is more probably due to delay in the passage of glucose through the liver. As stated above, epinephrine could not be relied upon to help in such an emergency.

It might be anticipated that, under such a disturbed condition of lowered storage capacity in the liver, increased storage might occur in the muscles. An observation of the arterio-venous sugar

difference during insulin activity was made in Case IV, as follows:

	Capillary Milligrammes *per centum*	Venous Milligrammes *per centum*
Blood sugar, 9.15 a.m.	419	402
50 grammes of glucose given 9.45 a.m.		
10 units insulin given 9.45 a.m.		
Blood sugar 11 a.m.	402	353

Estimations of basal metabolic rate have failed to show any evidence of an increased rate of oxidation in the muscles.

The third anomaly is the relative absence of ketosis observed in our patients (Charts I and II). We can find no record in the recent literature of patients having died in coma of the diabetic type, with high ketonæmia. Similarly the respiratory quotient, where this has been investigated, has not indicated any incomplete fat combustion. Stetson and Peters[1] are inclined to ascribe this peculiarity to an inability on the part of the damaged liver to elaborate ketones. The carbon dioxide combining power of the plasma in Case I, estimated shortly after the patient's admission to hospital, while he was dull and drowsy, with a blood sugar level of 280 milligrammes *per centum*, and very little acetonuria, was 20 volumes *per centum*. These findings should be considered in relation to the conception, held in some quarters, that the toxæmia of diabetic coma is not directly due to either ketosis or increased pH of the blood, but to some third factor, the concentration of which they together form the expression. Sheldon's patient[36] was aglycosuric and ketone-free though he showed a defective storage mechanism in his sugar tolerance curve. The most prominent symptom for the last two months of his life was intense drowsiness.

Natural History of the Syndrome.

A critical study of the available literature and a careful consideration of the cases here reported have brought us to certain conceptions regarding the nature and sequence of events occurring in *diabète bronzé*. In our opinion, the disorder probably occurs in three distinct phases: the pre-cirrhotic phase, the cirrhotic phase, and the terminal phase. These three periods may apply to any type of acquired hepatic cirrhosis.

The Pre-Cirrhotic Phase.

During the pre-cirrhotic phase the liver cells receive the initial injury which commences the vicious circle. It is generally assumed that the injurious toxin reaches the liver via the portal vein, as alcohol is known definitely to produce cirrhosis by this route. The fact that the most peripheral cells of the lobules are the most heavily pigmented, is said to support this thesis, though rabbits' livers became similarly impregnated following blood injections (Rous[7]). A review of the alcoholic intake of our own patients, and those reported in the literature, fails to impress us with its special frequency. The experiments of Mallory *et alii*, and of Hall and Butt,[21] are unconvincing as incriminating alcohol or copper as causal agents. This, of course, does not exclude alcohol as an aggravating factor in an individual patient. The nature of the toxin remains a mystery, whether chemical, bacterial, organic or inorganic.

The rôle played by acute fevers and syphilis seems negligible, though Evans has demonstrated a patient locally whose blood showed a triple positive Wassermann reaction. We must agree with the majority of observers, however (Mallory,[30] McCline,[32] Howard[33] and Stevens, Rosenthal[20]), that, initially, hepatic damage occurs; whether by portal or systemic route it is impossible to say. Donaldson[14] says truly that "the quest for ætiological factors is that of the larger quest for liver intoxications and cirrhosis in general".

The Cirrhotic Phase.

If we accept the theory that damage from a portal or circulatory toxin is sustained primarily by the liver parenchyma, we must then assume that it is of a special character, which causes a specific interference with the functions of the liver cells as regards the storage of metals, notably iron and copper, and as regards the retention and release of glycogen, as already explained. It is only in this way that the anatomy and physiology of the liver in hæmochromatosis differs as a rule from that of portal cirrhosis, especially the megahepatic or monolobular variety. Poulton and Cammidge[28] have recently expressed the view that certain functions of the liver cell may be lost without others becoming affected. It is not unreasonable to assume, following Kretz,[34] that a certain toxin may cause such selective damage, since iron deposition fails to appear following poisoning by arsenic or phosphorus, or in the hepatic degeneration associated with chronic venous congestion or cholecystitis. The only other clinical difference that occurs to us is the commoner development of mild jaundice and ascites in Laennec's cirrhosis, which may be related to a time factor, patients with hæmochromatosis frequently succumbing before such mechanical results of the cirrhosis become marked.

As in any chronic hepatitis, degeneration is ultimately followed by removal of the dead hepatic cells, and their replacement by a proliferation of the interlobular connective tissue. Cellular death and fibrosis then progress simultaneously, with attempts at fresh bile duct and parenchymatous regeneration taking place in the young connective tissue, until a uniform fine cirrhosis forms around islets of regeneration, and the whole organ becomes larger and tougher. Considerable argument has centred round the question as to whether the parenchymatous degeneration and subsequent fibrosis are the cause or result of the accumulation of iron within the liver cells. The consensus of opinion is that the cirrhosis is primary and the accumulation of pigment secondary. Rous and

Oliver's work[6] in rabbits showed that the mere accumulation of hæmosiderin in the cell is not capable of causing damage or death, and some cirrhosis occurred in only two animals. Some of the illustrations to this article show a degree and distribution of pigment indistinguishable from hæmochromatosis in man, but no increase in the interstitial stroma. Further, a varying degree of brownish discoloration of the liver due to iron, which occupies the same situation in the hepatic lobule, is fairly frequently found during autopsies on patients dying of portal cirrhosis (Kretz[34]), and has led to the use of the term "pigment cirrhosis" to describe this feature when well marked, but the relative amounts of iron and fibrous tissue are so disproportional as to make it most unlikely that the iron deposition has caused the cirrhosis. In hæmochromatosis the two features are more comparable in degree and progress together, but are probably both results of cellular damage from an obscure and hitherto elusive source (Muir). Stewart[11] disagrees with the majority of writers, who adhere to the cirrhosis-pigmentation sequence, on the grounds that cirrhosis of the liver could not have been present during the whole of the period required to store so much iron in the liver. He has published the result of autopsies on seven cases of hæmochromatosis, which show that while in the majority there was a close correspondence between the degree of siderosis and that of cirrhosis, in some siderosis was present, but very little cirrhosis. If we accept the above view that both are resulting from a common toxæmia, a relative preponderance of either element becomes comprehensible. It should also be remembered that any cirrhosis probably undergoes a very long latent period before becoming clinically obvious, and that by then the vicious circle is moving with much greater velocity than before, enhanced by the strangling effect of the mature fibrous tissue.

We must now attempt to discover whether any clue can be found in the information available as to the nature and distribution of the pigment in the body, whereby we can form an opinion as to the mechanism of its deposition. The following facts have been established in regard to the iron distribution in hæmochromatosis.

1. The liver contains the most iron of any organ (up to 100 times its normal content), the spleen comparatively little. The degree of pigmentation of the organs varies approximately according to their proximity to the liver in the body, especially the portal lymph glands (Rosenthal[20]).

2. The distribution of the pigment is, however, widespread. Sheldon has reported the most complete estimation of iron in the tissues, including the brain, and on clinical grounds we believe it is present in a diffuse form even in the retina and possibly in the mucous membranes. The spleen, bone marrow, kidneys and suprarenals are less heavily loaded than in conditions of blood destruction, such as pernicious anæmia, or hæmolytic jaundice, or following artificial blood injections (Rous and Oliver[6]). The condition of the pancreas has already been referred to.

3. There is no evidence pointing to excessive blood destruction as evidenced by anæmia, jaundice or great activity of the bone marrow.

It is apparently the duty of the liver cells to reexcrete any excess of iron over that required for hæmatopiesis or tissue repair, once the stores for iron are filled. The bowel mucosa absorbs all the iron and other related metabolic molecules up to a certain maximum. When these reach the liver cells, damaged in the specific manner we have assumed, it is probable that they remain there until the liver cell becomes stuffed with pigment; and then they are passed on into the general circulation to be stored in other cellular organs, including the pancreas, reached by way of the pancreatic arteries, and not the portal vein. The Küpffer cells remain relatively unpigmented, and probably function normally, but the liver cells, though able to form bile, cannot excrete metallic molecules, and so the latter gradually accumulate in the tissues, and especially in sites of old trauma, depending on their amount in the diet and the degree of damage sustained by the hepatic parenchyma as a whole. Rosenthal[20] is of the opinion that the inherent difficulty is loss by the liver cells of the power to convert ferric into ferrous salts, which he states to be the only form in which it can be utilized in the body, but does not explain how such an excess could be utilized and not either stored or excreted. The quantity of metal in the diet may further be influenced by the occupation of the individual.

The pigment is usually described as hæmosiderin, and this undoubtedly forms the greatest percentage of its composition, but it has been suggested that copper, and in all probability traces of other related metals, such as bismuth, zinc, manganese, nickel, *et cetera*, are contained in the pigment cluster (Funk and St. Clair[39]).

Mallory[30] killed rabbits after prolonged feeding with iron and copper, and the amounts of the two metals found in the liver seemed proportional to one another. In Rosenthal's[20] patient, the unpigmented malignant tissue was nearly copper-free, while the pigmented liver contained almost five times this amount. Rosenthal affirms that iron has a definite affinity for copper; and since both occur together in nature and are in excess together in the livers of the pregnant mother and fœtus and together facilitate hæmopoiesis, it is unlikely that the cells of the bowel or liver discriminate between them.

According to Donaldson,[14] the distinction between hæmofuscin and hæmosiderin is no longer to be maintained; hæmofuscin representing a stage in hæmosiderin formation and varying in relative concentration according to the technique in staining.

Experiments designed to demonstrate a negative iron balance have been contradictory, but the majority have shown a more or less complete retention of iron given by mouth (Garrod,[37] McCline,[32] Howard and Stevens[33]). Donaldson[14] has pointed out that these observers have not allowed for the latent time of excretion of iron. There can be no doubt, however, that the iron comes from the food. Observations of blood iron are equally inconclusive, as each worker assumes a different normal value. From the perpetuation of this valve-like action of the hepatic cells as regards metabolic molecules, the concentration of these elements in the tissues must be enormous. Attempts have been made to estimate the length of time required for the accumulation in the liver alone of the iron formation at autopsy, based on a daily retention of eight to ten milligrammes. These estimates vary from three years (Dunn[10]) to forty years (Howard and Stevens[33]). A clinical review would suggest about ten years as an average time. In this respect it is significant that no patient younger than thirty-one years of age appears in the literature. If the disease were an inborn error of iron metabolism (Dunn[10] and Sheldon[30]), one would expect an earlier appearance of pigmentation *et cetera*.

The Terminal Phase.

If the patient is not carried off by an intercurrent infection, aggravated by the hyperglycæmia, death occurs either from so-called hepatic failure or cholæmia, and from the appearance of a primary carcinoma of the liver, commencing in an islet of regeneration. This occurs with a frequency comparable with that following portal cirrhosis, 9·3% of 165 patients. The malignant cells are generally said to remain unpigmented, though Blanton and Healy report such as occurring in their patient. These stages are by no means fixed and consecutive, and are subjected to many individual variations, patients being frequently labelled as suffering from portal cirrhosis, *diabetes mellitus* and Addison's disease in earlier phases of their malady.

Expectation of life is similarly subject to great variation. Patients I and IV of this series are alive and their condition seems stationary after two and a half and two years respectively. Patients II and III died five and seven years after the recognition of their condition, which probably began even somewhat earlier.

The origin and nature of the skin pigmentation deserves separate mention. Golden brown granules occur in the corium and around the sweat glands, which resist the Perl stain. They are said to be melanin, due to the interference with the functions of the adrenal cortex, by the siderosis observed in the *zona glomerulosa* (Donaldson[14]). This is so sparse and scattered, however, and was absent in Rosenthal's case, that, remembering the wide margin of functional reserve possessed by the adrenal cortex (Swingle[42]), it is difficult to believe that such a mechanism occurs. Siderosis to a degree comparable with that seen in hæmochromatosis was observed in the adrenal cortex of rabbits after serial injections of blood without the appearance of pigmentation in the skin. It seems more likely that these granules are hæmofuscin, a stage in the evolution of hæmosiderin, and perhaps could have been demonstrated by hot stains, or else a melanosis comparable with that seen in other chronic diseases accompanied by cachexia.

Summary and Conclusions.

1. Clinical and biochemical findings in four patients suffering from hæmochromatosis are described.

2. Suggestions are made as to the natural history of the disease, which include the hypothesis of selective toxic damage to the liver, affecting the ability of the liver cells to store and release iron, related metals, and glycogen.

3. Since cirrhosis and pigmentation of the liver are the only features common to all cases, we are of the opinion that hæmochromatosis is merely a syndrome of liver cirrhosis in general and not a separate disease entity. It represents an advanced stage of "pigment cirrhosis".

4. The disturbance of carbohydrate metabolism is partly pancreatic, but mainly hepatic, wherein the extent of iron deposition is a fairly accurate index of the degree of interference with glycogenlysis and glycogenesis, possibly due to deficient formation of insulin kinase. In the few patients benefited by insulin, damage or dysfunction of the pancreatic islets is assumed to be present.

5. Prolonged epigastric pain is of evil prognostic omen.

6. We consider that further work in this field can be best applied in the direction of ascertaining the character of the iron and copper balance over an adequate period and by close biochemical investigation of the terminal coma of the disease, which clinically has points of difference from both true diabetic coma and cholæmia, together with further research on the glycogen and pigment metabolism in other types of liver cirrhosis.

Acknowledgements.

We desire to thank Dr. E. W. Fairfax, Dr. S. A. Smith, and Dr. C. B. Blackburn, under whose charge these patients were first admitted to hospital, for permitting us to observe and record their progress.

References.

(1) Richard P. Stetson and Henry W. Ferris: "Hæmochromatosis and Purpura", *Archives of Internal Medicine*, Volume L, August, 1932, page 232.

(2) J. W. Grieve: "Case of Hæmochromatosis", The Medical Journal of Australia, August 13, 1927, page 234, and December 17, 1932, page 758.

(3) E. H. Stokes: "Case of Hæmochromatosis", The Medical Journal of Australia, September 11, 1926.

(4) Eustace Russell: "Hæmochromatosis", The Medical Journal of Australia, March 14, 1925, page 251.

(5) D. M. McWhae: "Case of Hæmochromatosis", The Medical Journal of Australia, September 30, 1922.

(6) Peyton Rous and Jean Oliver: "Experimental Hæmochromatosis", *Journal of Experimental Medicine*, Volume XXVIII, November, 1918, page 629.
(7) Peyton Rous: "Urinary Siderosis", *Journal of Experimental Medicine*, Volume XXVIII, November, 1918, page 645.
(8) Humphrey Rolleston: Report of meeting of Section of Pathology and Bacteriology, British Medical Association, *The Lancet*, August 13, 1921, page 334.
(9) W. H. M. Telling: *The Lancet*, August 13, 1921, page 334.
(10) J. Shaw Dunn: *The Lancet*, August 13, 1921, page 334.
(11) M. J. Stewart: Report on discussion on liver disease, *The British Medical Journal*, December 2, 1922, page 1060.
(12) W. H. M. Telling and M. J. Stewart: Discussion on hæmochromatosis, *The British Medical Journal*, Volume II, 1921, page 783.
(13) John W. Orr: "Primary Carcinoma of the Liver in Case of Hæmochromatosis", *The Lancet*, June 28, 1930, page 1400.
(14) Robert Donaldson: "Case of Hæmochromatosis Complicated by Primary Carcinoma of the Liver", *Guy's Hospital Reports*, January, 1929, page 28.
(15) G. F. W. Hodges: "Bronzed Diabetes in a Woman", *The British Medical Journal*, March 2, 1929, page 396.
(16) Richard Stetson and John P. Peters: "Carbohydrate Metabolism in a Case of Hæmochromatosis", *Archives of Internal Medicine*, Volume L, August, 1932, page 226.
(17) Potter and Milne: *The American Journal of the Medical Sciences*, 1912, page 143.
(18) S. G. Shattock: *Proceedings of the Royal Society of Medicine*, Volume IX, 1916, page 49.
(19) W. B. Blanton, V. Richmond and W. Healy: "Report on Four Cases of Hæmochromatosis", *Archives of Internal Medicine*, Volume XXVII, 1921, page 406.
(20) S. R. Rosenthal: "Hæmochromatosis and Primary Carcinoma of the Liver", *Archives of Pathology*, Volume XIII, January, 1932, page 88.
(21) E. S. Mills: "Hæmochromatosis, with Special Reference to its Frequency and its Association to Women", *Archives of Internal Medicine*, Volume XXXIV, September, 1924, page 292.
(22) H. Barber: "Case Complicated with Primary Carcinoma of the Liver", *Guy's Hospital Reports*, January, 1929, page 46.
(23) G. R. Critchlow: "Case of Hæmochromatosis, Refractory to Insulin", *Proceedings of Staff Meetings, Mayo Clinic*, August, 1928, page 225.
(24) R. Wagner and J. K. Parnas: *Zeitschrift für die gesammte experimentelle Medizin*, Volume XXV, 1921, page 361.
(25) R. D. Lawrence: "A Case of Insulin Resistance", *The Quarterly Journal of Medicine*, Volume XXI, 1927, page 366.
(26) H. P. Himsworth: "The Activation of Insulin", *The Lancet*, October 29, 1932, page 935.
(27) J. Markowitz, F. C. Mann and J. Bollman: "Glycogen Function of Skeletal Muscle in Dehepatised Dog, with Special Reference to Rôle of Insulin Therein", *American Journal of Physiology*, Volume LXXX, 1929, page 566.
(28) P. Cammidge and E. P. Poulton: "Comment on Case of Dysinsulinism", *The Lancet*, March 11, 1933.
(29) A. B. Corkill: "The Influence of Insulin and Adrenalin on Carbohydrate Metabolism", The Medical Journal of Australia, October 17, 1931, page 477.
(30) F. B. Mallory, F. Parkes, Senior, and R. N. Nye: "Experimental Pigment Cirrhosis due to Copper, and its Relation to Hæmochromatosis", *Journal of Medical Research*, Volume XLII, 1921, page 461.
(31) E. M. Hall and E. M. Butt: "Experimental Cirrhosis due to Copper Poisoning: Its Relation to Hæmochromatosis", *Archives of Pathology*, Volume VI, July, 1928.
(32) W. Evans: Personal communication.
(33) C. W. McCline: "Metabolism in a Case of Hæmochromatosis", *Archives of Internal Medicine*, Volume XXII, November, 1918, page 610.
(34) G. P. Howard and F. A. Stevens: "Iron Metabolism of Hæmochromatosis", *Archives of Internal Medicine*, Volume XX, December, 1917, page 896.
(35) R. Kretz: *Zentralblatt für Allgemeine Pathologie und Pathologische Anatomie*, Volume VIII, 1897, page 620.
(36) Kempson Maddox: "The Retina in Hæmochromatosis", *The British Journal of Ophthalmology*, July, 1933, page 393.
(37) J. H. Sheldon: "Iron Content in the Tissues in Hæmochromatosis, with Special Reference to the Brain", *The Quarterly Journal of Medicine*, Volume XXI, October, 1927, page 123.
(38) A. Garrod: *The Quarterly Journal of Medicine*, Volume VII, 1913-1914, page 129.
(39) T. P. Sprunt: "Hæmochromatosis", *Archives of Internal Medicine*, Volume VII, July, 1911, page 75.
(40) C. H. Funk and H. St. Clair: "Hæmochromatosis: Report of a Case with Studies of the Copper Content of the Liver", *Archives of Internal Medicine*, Volume XLV, January, 1930, page 37.
(41) W. D. Keith and A. M. McNair: "Hæmochromatosis, Diabetes Mellitus and Primary Carcinoma of the Liver", *Canadian Medical Association Journal*, April, 1930, page 528.
(42) H. Root: "Insulin Resistance and Bronze Diabetes", *New England Journal of Medicine*, August 1, 1929, page 201.
(43) F. N. Allan and G. R. Constam: "Insulin Resistance in Case of Bronze Diabetes", *The Medical Clinics of North America*, Volume XII, May, 1929, page 1677.
(44) W. M. Swingle: "Function of Suprarenal Cortex", *The Lancet*, January 15, 1927, page 154.

Reports of Cases.

ERYTHRŒDEMA POLYNEURITIS (PINK DISEASE).

By James H. Younkman, M.B., B.S. (Adelaide),
Wagin, Western Australia.

On September 20, 1933, I saw B.C., a baby girl, aged ten months. She had been quite well until she was six months old, when her parents began to notice that she was limp and neither attempted to crawl nor to place any weight on her legs when held in a standing position. She frequently refused her food. She had slept well until six months of age, but since then her parents had to get up five or six times at night to cover her up, as she was sleepless and restless and uncovered herself frequently. When asleep she was often in unusual positions, for example, with her feet behind her ears. She had occasionally been irritable and had sometimes sweated profusely. There was no history of dribbling or scratching, but she rubbed her hands together frequently. The parents had taken no notice of the pink colour of her hands and feet.

I had seen the child two months previously with *otitis externa*. At this time there was certainly no redness of the hands and feet, and the parents had not started to worry about her limpness and did not mention it. Naturally I attributed the restlessness, irritability and insomnia then present to the infection. There had been no other illnesses.

On examination the child looked utterly miserable. She was sitting hunched up on her mother's lap and fell over when the support of her mother's arm was removed. The weight was 7·75 kilograms (fifteen pounds). The two lower incisor teeth had erupted. No abnormality was detected in the mouth, throat, ears, chest, abdomen or urine. There was a diffuse erythema of the cheeks with fine branny desquamation. The hands and feet were bright pink, swollen and quite cold. The colour extended 1·25 centimetres (half an inch) above each wrist and ankle. The skin felt thick, the swelling apparently being partly intracutaneous and partly subcutaneous. Sensation to pin prick was normal. All muscles were extremely soft and flabby. The knee jerks were not elicited. There was no photophobia.

The typical appearance of the hands and feet, together with the anorexia, muscular weakness and insomnia, constituted an unmistakable picture of pink disease. I am, however, of the opinion that the illness was a mild one.

Following the practice of Dr. S. F. McDonald,[1] the treatment adopted was: (i) Milk was given, at least one pint every day. (ii) Sunbaths were ordered. When first seen, the child had been having three-quarters of an hour in the sun each day. This was gradually increased to two hours. (iii) "Radiostoleum" (B.D.H.) was given in doses of 0·18 ml (three minims) three times a day. (iv) "Hepasol" (Glandular Preparations, Limited) was given in doses of four mils (two drachms) twice a day.

I did not consider it necessary to prescribe sedative lotions or hypnotics.

On September 27, 1933, the child attempted to stand when held up and the parents only had to get up to her once during the night. The appetite was still poor.

On October 4, 1933, the appetite was improving and the hands and feet were less pink and less cold.

On October 19, 1933, sleep was normal, the appetite nearly normal, and the weight 7·87 kilograms (fifteen and a quarter pounds).

On November 2, 1933, the hands and feet were almost normal, the weight was 8·08 kilograms (fifteen and three-quarter pounds), and the child was eating all her food and crawling.

On November 15, 1933, the child weighed 8·3 kilograms (sixteen and a quarter pounds) and was pulling herself up into a standing position in her playground. At this time I could detect no abnormality on examination.

Brain and Strauss[2] state: "The prognosis is good. Recovery is as a rule complete within from three to nine months." In this case complete recovery took eight weeks. It is quite possible that recovery occurred in spite of treatment, but the rapid improvement immediately following the exhibition of liver extract would seem to be more than pure coincidence, as Dr. McDonald suggests.

References.

[1] S. F. McDonald: "Swift's or Pink Disease: Recent Work on Pathology and Treatment", The Medical Journal of Australia, August 26, 1933, page 276.
[2] Brain and Strauss: "Recent Advances in Neurology", Second Edition, 1930, page 364.

UNUSUAL BLOOD SUGAR CURVES.

By Bruce Hunt, M.D. (Melbourne), M.R.C.P. (London),
Honorary Physician to Out-Patients, Perth Hospital and Children's Hospital, Perth.

On July 25, 1932, Mr. A.B., aged thirty-eight years, whose father had died of *diabetes mellitus* at sixty-three, was referred by Dr. W. A. Loftus, of Katanning, for an opinion as to diagnosis and treatment. Glycosuria had been found at an examination for life insurance three weeks before; during these three weeks the patient had been ordered a restricted carbohydrate dietary. Apart from the glycosuria there were neither symptoms nor signs suggesting *diabetes mellitus*.

A glucose tolerance curve (50 grammes) on July 26, 1932, gave the following results:

Time (hours)	0	½	1	1½	2	3
Blood sugar	130	240	280	230	210	180
Urine sugar	–		+		+	+

This curve was interpreted with a little hesitation as being probably due to a defect in glycogen formation, not to true *diabetes mellitus*; in other words, it was regarded as a glorified "lag" curve. The patient was advised to resume a full normal dietary, no restrictions whatever being placed on his carbohydrate intake. It was recognized that this was a somewhat unorthodox procedure, but it was thought justified by the complete absence of symptoms.

A repetition of the tolerance curve on October 3, 1932, the patient still being symptom-free, gave the following results:

Time (hours)	0	½	1	1½	2
Blood sugar	120	230	260	180	120
Urine sugar	–		+		+

This curve approximates a little more nearly towards the classical "lag" curve; it is possible that the antecedent carbohydrate restriction had slightly impaired the patient's tolerance on the previous occasion.

One year later, on September 28, 1933, the diet still being unrestricted and the patient still being symptom-free, a repetition of the tolerance curve produced the following most satisfactory results:

Time (hours)	0	½	1	1½	2
Blood sugar	120	180	210	150	90
Urine sugar	–		Trace		Trace

This is the typical "lag" curve of the text books and may be safely disregarded from the therapeutic and probably from the prognostic point of view.

Three points are brought forward by this series of observations.

1. Definite impairment of glucose tolerance is produced by a restriction of carbohydrate intake.

2. Of the two defective mechanisms in *diabetes mellitus*, glycogen formation and glucose utilization, it is failure of the latter which produces symptoms. In this case the former alone seems to be inefficient. In view of the family history it is suggested that the factors controlling these two processes may be inherited separately.

3. The greatest care should be exercised, no matter what the biochemical findings, before a patient whose only symptom is glycosuria is condemned to live under a diabetic *régime*.

Reviews.

VACCINE THERAPY.

"Vaccine Therapy in Acute and Chronic Respiratory Infections", by Henry T. Gillett, represents an attempt to establish the value of the administration of vaccines, not only in the treatment of septicæmia, all varieties of pneumonia, and chronic infections of the bronchi, naso-pharynx and nasal sinuses, but also prophylactically in influenza, chronic bronchitis and recurring and chronic infections of the upper respiratory tract.[1]

It is claimed that if the vaccines be prepared and administered in the manner advised, the mortality in Type I lobar pneumonia, treated during the first three days, can be reduced to 5% as compared with a mortality rate of 12% in similar cases treated by serum.

It is also stated that cases of chronic post-nasal catarrh, sinus infections, and acute and chronic bronchitis can be greatly benefited and generally cured by treatment with an appropriate stock or autogenous vaccine.

The results claimed are much better than those obtained by other workers, by this or any other method of treatment. The author apparently supports the statement of Dr. Georges Rosenthal, whom he quotes, "that those who do not use vaccines in acute pulmonary disease are guilty of criminal neglect."

The method of preparing the vaccines and details of their administration are clearly set out, and one feels, after reading the book, that, despite previous disappointments, the method of treatment advocated might be given a further trial.

Statistics are quoted which seem to prove that prophylactic vaccination is of great value in influenza. This is contrary to the general experience in Australia during the last pandemic.

BIOLOGICAL CHEMISTRY.

Parson's "Fundamentals of Biochemistry" is a somewhat elementary introduction to the study of biological chemistry.[2] In this fourth edition the author has brought his material thoroughly up to date. This is an excellent book, and in the 400 pages the author covers a surprising amount of ground with a high degree of accuracy. The treatment is necessarily somewhat dogmatic, but the English is so good and the style so lucid that it can be read very easily.

An elementary knowledge of organic chemistry is assumed, but this need be only very elementary, for the author develops the formulæ of substances of biochemical interest in a remarkably clear manner. An excellent feature is the use of large clear type for all chemical formulæ. Another useful feature is the introduction of comprehensive charts showing, for example, the changes undergone by carbohydrates in the muscles, liver, alimentary canal, fat depôts and mammary glands, and the interrelationships of these.

At the end of each section is a short, but well chosen, bibliography to aid the student who wishes to read further. This book can be confidently recommended to anyone as a very readable and accurate account of the present position of biological chemistry.

[1] "Vaccine Therapy in Acute and Chronic Respiratory Infections", by H. T. Gillett, M.D., with a foreword by W. H. Wynn, M.D., F.R.C.P.; 1933. London: H. K. Lewis and Company, Limited. Crown 8vo., pp. 116, with nine charts. Price: 5s. net.

[2] "Fundamentals of Biochemistry in Relation to Human Physiology", by T. R. Parsons, B.Sc., M.A. Fourth Edition; 1933. Cambridge: W. Heffer and Sons Limited. Crown 8vo., pp. 447. Price: 10s. 6d. net.

The Medical Journal of Australia

SATURDAY, APRIL 7, 1934.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.

BROADCASTING AND MEDICINE.

THE present is an age of rapid development; the marvel of today is the commonplace of tomorrow, and the commonplace soon becomes a necessity. The development in turn of telegraphy, of telephony and of radio-transmission has been rapid. They have annihilated distance, they have shortened time and they have brought the nations of the earth closer together. It would be difficult to imagine a return of humanity to a life devoid of even one of these means of communication. Few people possibly stop to consider how complete is the network of telegraph, telephone and wireless communication. The cables from every country in the world, printed in the morning newspaper, are taken as a matter of course, but it may come as a surprise to many to know that every telephone subscriber in Australia can be connected to any one of 32,500,000 telephones or 92% of the telephones of the world. Though figures are not available for the number of wireless receiving sets in different countries, we have it on the authority of the "Commonwealth Year Book" that in the year 1931-1932, 369,072 licences for wireless sets were issued in the Commonwealth. This represents roughly an increase of 38,000 on the total of the previous year. Before long very few homes will be without a wireless installation.

The telegraph and the telephone may be regarded as means of communication between persons or groups of persons. By radio-transmission, however, one message may reach many thousands of listeners. Given suitable atmospheric conditions, a messsage may be heard in every one of 369,072 dwellings in Australia. Broadcasting by wireless is used for purposes of entertainment, of education, and of advertisement. These three functions, of course, are not distinct and separate, for an advertisement may be both entertaining and instructive. Education also (and this is of importance in our present discussion) can be made entertaining. It is therefore obvious that a great responsibility devolves upon those who have control of broadcasting. This is a matter that concerns intelligent people. In a leading article on broadcasting in a recent issue of *The Times Literary Supplement* it was stated that "the more technology moves forward, so much the less ought finer minds to say 'This is no place for us,' but, if the world is to be habitable, ought rather to go forward themselves and attempt to preside over the development". There is no gainsaying the truth of this. In its application it must be remembered that finer minds are as a rule specialized in certain directions. Although a person may be highly cultured in one direction, he may be curiously deficient of a sense of values in another. The devotees of every cultural and educational activity should interest themselves in radio-transmission.

The medical profession in the early days of wireless showed a remarkable lack of initiative in regard to the radio-transmission of teaching in matters of health. Education of the public is a catch phrase dear to the medical ear. Like other catch phrases, it slips easily from the tongue, and is sometimes used as the crowning platitude to a collection of platitudes presented to a medical gathering in the form of a paper. There has always been a fear, sometimes, but not always, expressed, that the practitioner doing the teaching may be gaining an indirect personal advertisement, and

sometimes there has been the implication that teaching was being given solely with the object of securing advertisement. In spite of these fears and implications, the medical profession has more or less awakened to its duty and to the possibilities of wireless transmission. In several States of the Commonwealth wireless talks on health are given by medical practitioners. These talks may be considered from the point of view of the medical practitioner and of the bodies controlling radio-transmission. The medical practitioner's point of view need not be discussed at length, though much might be written on the kind of teaching given and on the manner of its presentation. At present health talks are best given by officials of health departments or by university teachers not engaged in private practice, for the public naturally likes to know the name of the man addressing them. At the same time the Branches of the British Medical Association might all adopt the measure, already used by some of them, of appointing some of their members to speak anonymously with the authority of the Branch. In these circumstances the Branch should approach the broadcasting authority in the State and ask that arrangements for such talks be made. From the other point of view, that of the broadcasting authority, action should be taken to limit to qualified medical practitioners the giving of advice on health. The Federal Council of the British Medical Association in Australia recently sought to have this restriction brought about. The Director-General of the Postmaster-General's Department wrote asking for definite instances in which broadcasts were considered misleading and harmful. Obviously the Federal Council could not do this. In this country any unqualified person is allowed to treat disease, provided he does not lead people to believe that he is a medical practitioner. In wireless talks advice on health matters purporting to come from medical practitioners is given by non-medical persons. The position, to say the least of it, is anomalous. It is the duty of the health department in each State to foster the public health. If a State department were to give information to the Postmaster-General regarding misleading health talks, he might be induced to act.

Current Comment.

PAIN AS AN INDEX OF DISEASE.

One of the most important of all symptoms which bring patients to doctors is pain. A great amount of attention has been paid to the radiations and surface reflections of pain, but perhaps less interest than the subject deserves has been bestowed on the various types of painful sensation. Another very important aspect of pain concerns the sensitiveness of the individual to severe or unpleasant stimuli. No clinician can fail to be impressed by the extraordinary difference in the degrees of pain described by patients who are apparently suffering from lesions that should evoke similar degrees of thalamic disturbance. Certain of these aspects of the subject have recently been discussed by the Section of Gastro-Enterology and Proctology at the recent annual session of the American Medical Association.[1] Emanuel Libman, who has previously advocated some definite standard by which a patient's sensitiveness to pain may be estimated, in particular his test of pressure over the styloid process near the angle of the jaw, brings out some points of importance. Whether the test that he has propounded represents a reliable estimate of sensitivity or not may not be open to question, as was apparent in the discussion, but a very significant experience of Libman, reinforced by other clinicians of note, is that the hyposensitive patient may have so-called substitution symptoms. In the case of visceral disease this is very important. Thus the person who reacts markedly to painful stimuli may complain bitterly of pain arising from, say, a gastric ulcer, and this complaint may "cover" other reflex symptoms due to disturbance of the autonomic nervous system. On the other hand, the hyposensitive person will in all probability describe phenomena like a feeling of pressure, flatulence, nausea *et cetera*, but make little complaint of pain. This factor in symptomatology is rightly stressed, for it is often overlooked. Of course, it must be recognized that the pathological conditions underlying a morbid state are not always the same; also a predominant symptom like dyspnœa will, by its very nature, occupy some of the field of consciousness that otherwise would be more or less filled by pain. This latter fact is clearly pointed out by Libman. He also remarks that the subject is still a fruitful one, albeit difficult, owing to its subjectiveness. His suggestion of the study of the relative importance to the brain of all symptoms is also of value, and more work might be done on these lines.

B. D. Crohn, in adding to the discussion, states that the two elements concerned in the appreciation of pain by the individual are the varying reception in the neural centres of the stimuli, and the factor due to psychic causes; this puts the same idea in

[1] *The Journal of the American Medical Association*, February 3, 1934.

clear terms. He also brings forward statistical evidence to prove that serious complications, such as hæmatemesis and perforation, are more likely to occur in gastric ulcer in the case of persons who are found on test to be hyposensitive. This accords well with what we should expect if we regard pain as a primitive protective mechanism.

W. C. Alvarez, in the course of some supporting remarks, suggests that one reason why cancer of the stomach is so often diagnosed too late is that the patients are often relatively insensitive and may be seriously ill before seeking advice.

The whole of this interesting discussion cannot be traversed here, but reference should be made to the insistence on the importance of the segmental nature of visceral pain by Pottenger. This writer also refers to the differences between acute and chronic pain, in particular with regard to the lowering of the pain threshold by repeated attacks of a painful ailment. In connexion with the investigation of pain and tenderness of the abdominal wall, J. B. Carnett makes some useful observations. For instance, he points out that pain and tenderness in the parietes are best demonstrated while the patient balloons out the abdominal wall, this manœuvre guarding the viscera from interference while the observer carries out his examination. He also pays tribute to the value of the pinching test, where the superficial tissues are firmly and sharply plucked up; this, as he says, is undoubtedly of much greater clinical use than a pin test where the question of abdominal visceral disease must be decided. He stresses the importance of distinguishing between pain arising from the parietes and from the viscera; all physicians and surgeons are alive to this, but it is valuable to attempt to arrive at some definite procedures by which this may be done.

It will be seen that these observers are endeavouring to bridge one of the huge gaps that exist in clinical medicine and to evaluate the significance of pain. This, of course, depends to a great extent upon the individual judgement of the medical practitioner, but any attempts to establish a sounder scientific basis for this judgement are most welcome. Another most valuable contribution to the general subject of pain has been made recently by Sir Thomas Lewis.[1] He has investigated both on the clinical and experimental side the question of "burning" pain, particularly in the extremities. He is interested particularly in the ultimate mechanism by which the actual stimulation of the end organ takes place, and sets forth some definite ideas, which seem to be shaping towards an hypothesis. He distinguishes between a painful sensation of brief duration, due probably to direct physical or physico-chemical stimulation, and one of a "smooth" type, more gradual in onset and more prolonged in experience. The latter he regards as due to a metabolic and diffusible chemical cause. This leads to the concept of a "pain substance". In the particular varieties of pain studied he has carefully reviewed cases of circulatory disturbance in the extremities of many kinds, including both the functional and organic. He concludes that the painful redness seen in a dependent limb is associated with a capillary tonelessness and congestion rather than true vaso-dilatation. A certain susceptible state is, however, necessary to produce the characteristic burning pain, though he believes that in all such cases the underlying cause for this pain is the release from damaged tissues of a substance which acts on the pain nerve endings and, by lowering their threshold to stimulation, makes pain impulses arise from otherwise normal conditions of tension or temperature. Here we have the dual concepts of the necessity for recognizing (and, if possible, calibrating) a threshold and the value of postulating a definite physical or chemical cause for pain. This subject is within the reach of all clinicians, and it is to be hoped that the future will see further return to the study of pain. The diagnosis of internal disease cannot be made by mechanical means, but the richer the accumulated knowledge available to the medical public, the less difficult will be the solution of that often embarrassing question: "How severe is this patient's pain, and what does it betoken?"

[1] *Clinical Science Incorporating Heart*, Volume I, Number 2.

A JOURNAL DEVOTED TO LEPROSY.

The International Leprosy Association, with the aid of the Leonard Wood Memorial Fund, has established the *International Journal of Leprosy*. The first number, bearing the date January, 1933, has come to hand. Many medical practitioners in Australia are interested in leprosy and some have made contributions to literature on the subject. They will be glad to know of the new journal. The journal is controlled by an editorial board and contributing editors have been appointed from a great number of centres in different parts of the world. Australia is not mentioned in the list. Apparently no Australians belong to the International Leprosy Association. This state of affairs should be remedied. The address of the journal office is: P.O. Box 606, Manila, Philippine Islands.

AN EXAMPLE TO HOSPITALS IN NEW SOUTH WALES.

Many medical practitioners object to the establishment in public hospitals of wards for private patients, on the ground that none but members of the honorary staff will be permitted to attend patients in these wards. We therefore note with satisfaction that the Board of the Royal Alexandra Hospital for Children, Sydney, has decided that all medical practitioners shall have the right to attend in the private and intermediate division of the hospital their own patients suffering from non-infectious conditions. Until an operating block is built, this provision will apply only to patients with medical conditions.

Abstracts from Current Medical Literature.

MEDICINE.

Collapse in Diabetic Coma.

M. LABBÉ AND R. BOULIN (*La Presse Médicale*, November 4, 1933) consider collapse to be the principal cause of death in diabetic coma; and not in elderly patients only, but also in the young with no previous indication of heart affection. Consequently, the blood pressure should be examined as scrupulously and as frequently as the urine throughout the duration of the coma and for at least twenty-four hours after the disappearance of acidosis and the recovery of consciousness. Collapse may occur at the onset of coma, more frequently six to seven hours and sometimes thirty-six hours after the onset. The precursory signs of collapse are diminution or suppression of urine and fall of blood pressure. The latter may come on very rapidly and the systolic pressure may fall in half an hour from 120 to 70 or 50 millimetres of mercury and become too low for estimation, the radial pulse at the same time becoming impalpable. Up to this stage the pulse is regular and the rate not accelerated beyond 130. The heart sounds remain distinct and there are no signs of circulatory embarrassment in the lungs, liver or soft tissues. Apart from the anuria, fall of blood pressure is the only indication of the grave condition of the patient. In the treatment of this condition cardiac stimulants, such as digitalis and "Ouabain", have been of little value. The authors cite a paper by Lawrence, who suggested that dehydration consequent on polyuria, diarrhœa and vomiting is a main factor in producing collapse. Lawrence treated his desperate cases with copious intravenous injections, using hypertonic saline and gum acacia solution. The authors doubt whether dehydration is as frequent and important as has been urged; and they suggest that in Lawrence's two cases recovery was due not so much to relief of dehydration as to the use of adrenaline in the intravenous injections. This they regard as the remedy *par excellence*. They treated two patients with intravenous injection; in the first case they used three milligrammes of adrenaline in two litres of normal saline solution, and in the second, one milligramme in 0·5 litre. The injections were given slowly, occupying more than two hours in the first case and nearly one hour in the second. In both cases improvement was almost immediate. In any case of coma, if the systolic pressure falls to 100, intramuscular injection of adrenaline or ephedrine should be used. If the pressure falls below 90 millimetres of mercury, there should be no delay in giving an intravenous injection of one litre of warm physiological saline solution with one milligramme of adrenaline. And this should be repeated, if necessary, several times. Subsequently the blood pressure should be observed for some days, and if it tends to fall, intramuscular injections of adrenaline or, preferably, of ephedrine should be given.

Heart Block in the Young.

I. I. LEMANN (*Annals of Internal Medicine*, December, 1933) analyses the details of 100 reported cases of atrio-ventricular block occurring in patients below the age of thirty years. The frequency with which heart block occurs in the young is surprising, as also is the lack of severe symptoms in the majority and their ability to carry on the most strenuous lives. In many bradycardia is the only finding, often discovered accidentally during routine examination. Stokes-Adams syndrome was present in a minority of the cases under review. The prognosis is much less serious than would have been anticipated so far as permanent blocks are concerned, the condition being known to exist for years in many cases of this collection. As for the ætiology, it is necessary to look for causes entirely different from those found in elderly patients: arteriosclerosis, coronary disease and myocardial fibrosis. The following seem to be the most important: (i) Acute infections, especially diphtheria, influenza, and typhoid fever; (ii) rheumatism; (iii) congenital abnormalities (some 42 of this series belonged to this group). Unfortunately only four autopsy findings are recorded, septal defects being found in each instance.

Jaundice in Exophthalmic Goitre.

DONALD C. BEAVER AND JOHN DE J. PEMBERTON (*Annals of Internal Medicine*, December, 1933) discuss the pathological basis of icterus occurring in 23 of 107 consecutive cases of exophthalmic goitre. Those cases thought to represent previous or independent hepatic and biliary obstructive disease have been excluded. Five cases were associated with passive congestion of the liver of a relatively severe grade. The explanation of this sign in the remaining cases seems to depend on the clearly demonstrable alterations in hepatic tissue which, according to the authors' conclusions, are an integral part of the pathology of exophthalmic goitre, and they are due directly to thyreoid intoxication, since they are usually intimately related in their severity to the intensity and duration of the disease. Three types of hepatic lesion are described: (i) acute degenerative lesions (fatty metamorphosis, focal and central necrosis and changes secondary to stasis of blood); (ii) simple atrophy; (iii) subacute toxic atrophy and toxic cirrhosis. The cirrhosis is termed by Weller an interlobular chronic parenchymatous hepatitis, characterized by lymphocytic infiltration, bile duct proliferation and increased stroma in the islands of Glisson. This picture differs from the usual atrophic cirrhosis in its more irregular distribution. The hepatic lesions are adequate to account not only for the presence of icterus, but also for the disturbance of hepatic function, detectable by hepatic efficiency tests, occurring in 40% of the cases of this series.

Myocardosis.

W. L. BIERRING (*The Journal of the American Medical Association*, August 26, 1933) discusses myocardosis, a term suggested by Riesman in 1926, to indicate the chronic non-valvular heart disease of adults. This name was applied to those varieties of cardiac incompetence which are frequently called myocardial degeneration. The basis of these conditions is either infective or vascular, mainly vascular. The symptoms are often vague, but palpitation, breathlessness and substernal discomfort are significant. Heart lesions associated with coronary artery disease are included. Certain changes in the electrocardiograph are thought to give some clue to the diagnosis, but, apart from those of coronary disease, are not diagnostic. The management of the patients is mainly in the direction of rest with sufficient mild regular exercise.

Lead Poisoning.

E. BASS (*Deutsche Medizinische Wochenschrift*, November 3, 1933) discusses the relation of the clinical picture of lead poisoning to the lead content of blood and urine. In healthy persons who have had no occupational contact with lead an average amount of lead in 100 cubic centimetres of blood or in 1,000 cubic centimetres of urine is 0·02 milligramme. An increase to 0·06 milligramme in the blood and to 0·1 milligramme in the urine is generally accompanied by clinical signs of lead poisoning. Among the 40 patients who were investigated, three patients who had "recovered" from lead poisoning still showed 0·07 milligramme in the blood and 0·13 to 0·16 milligramme in the urine. This persistence was probably attributable to lead depôts in the body from which lead was being passed into the blood and excreted in the urine. In 13 cases of definite lead poisoning the relation of the several usual signs to the lead content of the blood and urine was studied. The lead line was present in seven of these, absent in six. Of the seven with the lead line, five had blood lead 0·06 to 0·47 milligramme and urine lead 0·07 to 0·26 milligramme, and two had blood lead below 0·02 milligramme and urine lead 0·09 and 0·22 milligramme respectively. One patient with no lead line had blood lead 0·12 milligramme. The author remarks that the lead line is not a delicate indicator of fluctuation in the blood lead level and may persist when the blood lead has become normal. Anæmia (a hæmoglobin value of 80% or less) was found in seven cases of this group. In six of these the blood lead was high, 0·06 to 0·47 milligramme, the urine lead 0·1 to 0·148 milligramme. The grade of

anæmia does not always correspond to the blood lead and still less to the urine lead. In one case the hæmoglobin value rose from 65% to 85% without any change in the blood and urine lead. Long-continued poisoning of even minor degree causes more severe anæmia than does a higher lead value of recent occurrence. Basophilia was found in only five of these thirteen cases, usually accompanying anæmia and never with a blood lead of less than 0·06 milligramme. Porphyrinuria had an ill-defined connexion with lead. It was found in five cases with raised blood and urine lead, but was absent in two cases in which the blood lead was 0·14 and 0·12 milligramme and the urine lead 0·18 and 0·48 milligramme. Colic was the commonest subjective symptom. In only three of the thirteen cases was it absent. Curiously, two of these three had raised blood lead, and, on the other hand, several patients with colic had blood and urine lead near normal. Nerve lesions were found in only four of the thirteen cases. In two of these the blood and urine lead was raised; in the other two it was not. It appears certain that the development of these lesions takes a much longer time than does the elimination of the lead from the body. Renal inadequacy was found in three cases. All had considerably raised urine lead and two had raised blood lead. Another patient with all the signs of chronic contracted kidney had the blood lead only slightly raised and the urine lead not at all raised. The author considers that frequent estimation of lead in blood and urine is the only means of following the gradual elimination of the lead and of estimating the efficacy of treatment.

Dinitrophenol in the Treatment of Obesity.

W. C. Cutting and M. L. Tainter (*The Journal of the American Medical Association*, December 30, 1933) offer the results of eight experiments on four subjects on balanced and unbalanced diets in support of the use of α-dinitrophenol (1-2-4) in the treatment of obesity. The unbalanced diets were abnormal in containing a maximal tolerated amount of carbohydrate, protein or fat, but were adequate as to caloric content on the basis of a normal metabolic rate. A normally balanced diet was used for comparison. After a week of control observation on the particular diet, α-dinitrophenol, 225 milligrammes in capsule (the single daily dose) was given by mouth before breakfast for a period of from seven to sixteen days. The dose was increased on occasion to 300 milligrammes during the second week. In every case there was an increase in the basal metabolism by from 30% to 50%. The subjects excreted less nitrogen than they ingested, yet there were definite losses of body weight. Therefore body proteins were not broken down. The output of urinary organic acid was not increased, indicating that the fats were completely burned without giving rise to acidosis. Metabolism is increased regardless of the energy materials of the diet, though the burning of the carbohydrates or fat is primarily promoted, provided that the diet is of adequate caloric value. The rise of metabolism is prompt and vigorous, and there are no disturbing subjective symptoms. Dinitrophenol is indicated clinically in obesity and may be useful in other conditions of depressed metabolism. It appears to be relatively safe for as long periods as have so far been studied. There appears to be an incidence of 5% to 6% of dermatitis, which promptly ceases on withdrawal of the drug. No restriction of fluids is necessary.

The Changing Aspect of Tuberculosis Treatment.

J. Burns Amberson (*The New England Journal of Medicine*, October 19, 1933) discusses recent changes in the attitude towards the treatment of pulmonary tuberculosis. These are largely the result of our knowledge of the evolution of the disease, especially in its early stages, through radiographic evidence, and of our ability more accurately to decide the probable fate of the individual patient. The author regards it as essential that serial X ray films be taken to guide in treatment, symptomatic indications alone being crude and unscientific. The most decided changes now being witnessed in the management of tuberculous cases are the wider and more prolonged use of bed rest, and the earlier and more judicious application of collapse therapy. Almost every patient in whom incipient tuberculosis is found should be promptly put to bed. Rest should be continued until it has been demonstrated by serial skiagrams that healing is progressing, even though symptoms are absent. By this method healing is often complete and collapse therapy is not required. Individual experience will enable the physician to decide what patients will require immediate collapse therapy, of which the ideal method is artificial pneumothorax. Immediate symptomatic amelioration is not sufficient, as there may be inadequate healing of the pulmonary lesion, with subsequent relapse. Artificial pneumothorax is the surest means available for obtaining permanent healing of the pulmonary lesion. The employment of other surgical procedures is increasing and results are becoming increasingly satisfactory. The need is for medical and surgical judgement to assure the most discriminating and judicious application of the many forms and combinations of treatment now available.

Pulmonary Tuberculosis in Adolescents.

Alton S. Pope (*The New England Journal of Medicine*, October 19, 1933) has made a study of pulmonary tuberculosis in children of school age from the standpoint of frequency, diagnosis and prognosis. Notwithstanding an equal rate of infection in males and females, up to 50% at the end of school life, as shown by tuberculin tests, pulmonary tuberculosis was found in an increasingly greater proportion of the infected girls than of the infected boys. In Massachusetts, where the study was made, it was found that between the ages of ten and nineteen pulmonary tuberculosis took a toll of more than three times as many deaths as all the acute communicable diseases combined. The diagnosis of the disease in children in the early stage is almost entirely dependent on competent radiological examination. A careful study of one thousand students revealed manifest tuberculous disease in fifteen. In none of these were any symptoms or signs found, while among twenty-four in whom suspicious physical signs were detected, none proved to be suffering from tuberculosis. The author concludes that the only practical method of discovery of the disease is X ray examination, and that waiting for the development of symptoms and signs before starting treatment in a child of school age who shows tuberculous infiltration, is likely to throw away the patient's only chance of recovery. In a group of 88 school children in whom a diagnosis of pulmonary tuberculosis had been established four to eight years previously, there was found to be a subsequent mortality of 28%. In two groups of children in hospital with pulmonary tuberculosis between 1910-1920 and 1920-1927 respectively, the mortality was found to be 80% and 68%.

Pituitary Hormone.

M. B. Sulkerger (*The Journal of the American Medical Association*, June 17, 1933) describes the use of a new pituitary hormone, intermedin, secreted by the *pars intermedia* of the pituitary gland. Zondek has shown that intermedin changes the pigment of *Phoxinus lævis*, a type of minnow, causing red to appear on the belly and other parts. This pigment reaction was used to standardize intermedin preparations, and the quantities of hormone in solution were expressed in phoxinus units. The author used intermedin in the treatment of two patients with *diabetes insipidus*. The lesions in this disease are localized in or about the pituitary gland, and extract of posterior lobe of the pituitary gland controls thirst and urination in this condition. Zondek has shown that this extract contains large amounts of intermedin. In the two patients treated, one to two cubic centimetres of intermedin were injected deeply in the subcutaneous tissues. The result was an immediate reduction in the frequency of urination and in the thirst. After the injection the patients urinated at normal intervals, whereas previously urination was necessary every hour or less. Intermedin caused no ill effects.

Special Articles on Treatment.

(Contributed by request.)

XXIX.

THE TREATMENT OF INGROWN TOE NAIL—INGROWING TOE NAIL—PARONYCHIA.

It would be well to bear in mind at the outset that the lay term, ingrowing toe nail, is a misnomer. Even though the configuration of the nail may somewhat alter, the nail edge does not grow in, but rather is there a heaping-up of inflammatory tissue which overlaps its dorsal and lateral surface.

The condition of ingrowing toe nail may occur in any of the toes, but it is chiefly associated with the great toe, and it is in the latter situation that the lesion will be discussed here. The anatomy of the nail bed is broadly similar in the hand and in the foot, and a clear knowledge of its architecture is necessary to an understanding of the treatment of ingrowing toe nail. The crescentic, opaque, white portion towards the base of the nail is the lunula, whilst the portion beyond the lunula is the body of the nail. Subjacent to the lunula is the nail matrix, and nail growth is from this matrix epithelium. Full nail thickness is not attained until we reach the distal part of the lunula, whence it continues at a regular thickness. From the distal portion of the lunula there is a gradual decrease in the thickness until the proximal end is reached, and it is possible that this accounts for the opacity of the nail of the lunula. A cross-section of the body of the nail or of the lunula will show a chisel edge on either side. Dorsal to the nail root is the eponychium, a tongue-like structure consisting of epithelium on the dorsum, which turns sharply back where it meets the nail, as the "reflected layer" of the epithelium, to fuse with the proximal edge of the matrix, constituting the nail sulcus. Between the reflected layer and the dorsal epithelium is a tongue of subcutaneous tissue. In continuity with this eponychium on either side of the nail lies the paronychium of similar structure. These tissues are freely supplied with sweat glands, and these may be a factor in the extension of superficial infections. Beneath the nail-bed lies the subungual space, which is highly vascular.

Next to anatomy, an understanding of the causation is necessary for a knowledge of treatment. Prominent as a causal factor is lateral pressure, which is brought about in a number of ways, but chiefly by hose and footwear. At first the paronychium on either one or both sides of the nail becomes moulded against the adjacent structure, on the one side the shoe, and on the other side the second toe. The transverse arch of the nail becomes exaggerated. The dorsal portion of the paronychium bulges and the compressed part becomes actually thinned. Gradually the nail edge breaks through its sulcus epithelium and infection is superadded. Repeated infections cause scar formation and a chronic paronychia results on one or both sides of the nail. The overgrowth of granulation tissue and the inflammatory swelling tend to increase lateral pressure and the vicious cycle continues.

The organisms most commonly involved are *Staphylococcus aureus* and *Staphylococcus albus* and, less commonly, the varying types of streptococcus. Still less common, we have the yeast-like organisms (monilia).

It may be broadly stated that practically all cases of paronychia yield to conservative treatment, but since the conservative treatment must be long continued, many patients find it tiresome and ultimately prefer radical treatment. Since lateral pressure is so prominent a feature in the causation, the removal of this factor constitutes the first and most important feature in treatment. Hose is frequently a factor here, and it will be found an advantage to wear hose giving ample space for free movements of the toes. It would be more correct anatomically if hose were made with right and left types, as is done in the case of our footwear, which would then allow ample room for the great toe. But as these are commonly unprocurable, an approximation can be obtained by wearing loose hose a size or two larger than is normally used. It may be found an advantage to change the hose more frequently than is the custom. The hose should preferably be light, permitting ventilation. Advantage may also be taken of any opportunity to go bare-foot. Shoes should conform to the normal posture of the foot and should, therefore, be straight on the inner side as far as the end of the great toe, and should be sufficiently loose across the toes to allow for free movements of the toes, especially spreading movements. Account may have to be taken of any associated foot deformity which would tend to cause this lateral pressure. Thus an associated *hallux valgus* is a frequent factor in paronychia of the outer side of the nail, and in certain cases some treatment of the *hallux valgus* would be indicated before success will be attained in the treatment of the associated paronychia. *Pes plano-valgus* is also a factor in lateral pressure, through the associated incorrect stance. Here again the treatment of this condition may be a necessary concomitant. Particularly is correct stance of value. While in native races it has been shown that there is some variation from the parallel alignment of the inner aspect of both feet in stance and in walking, this position should be aimed at and, if necessary, by an elevation of the inner side of the heel by means of a *valgus* wedge of approximately six millimetres (one-quarter of an inch). The latter procedure is more effective if the outer side of the heel be shelved.

Particular care must be taken with the cutting of the nail. A common form of trauma of the nail sulcus and paronychium is the incorrect use of scissors in cutting short the lateral edge of the nail, and this trauma is a factor in the subsequent infection. The nail should be allowed to grow to a substantially free end and should be cut only as it tends to overlap the subjacent soft parts distally. Thus at the side there should be a considerable overlapping free edge. No attempt should be made to cut into this portion. It is sometimes recommended to pare down the centre of the nail in its distal portion or cut a triangular piece in this situation. But this is not necessary. In the average case the removal of all lateral pressure and the correct cutting of the end of the nail will be all that is necessary, provided the subject has patience. As the new nail gradually grows distally without the superadded trauma, so the lesion will, in most cases, slowly heal proximo-distally.

In any average case of paronychia, where the lesion is not extreme, local applications are not of great value beyond the aspect of personal cleanliness and comfort. This is largely due to the fact that the infection, sometimes accompanied with pus formation, generally extends under the nail, so that discharge has no satisfactory outlet and antiseptics do not reach adequately the affected area. Conservative treatment as a rule will take some months for a successful conclusion. Difficulty will be found in inducing certain patients to wear satisfactory footwear. For these, and for some with the more advanced cases with pus formation under the nail, operative treatment may be indicated. A simple incision for pus is rarely indicated and should be done only where there is no extension of pus under the nail. Such incisions should on no account pierce the matrix, as this generally causes a permanent deformity of the nail. A simple procedure, if this lesion be not advanced, is the removal of sufficient nail to allow full drainage, by an incision running proximo-distally, parallel with the lateral portion of the nail sulcus. This would presuppose the wearing of correct footwear afterwards.

A somewhat more radical procedure is necessary where custom shoes must be worn by the patient. This consists of removal of a portion of the nail and the corresponding portion of the nail-bed. Great care must be taken to remove the whole of the nail-bed matrix from the area of operation. This operation permanently narrows the nail. An oblique incision is made through the nail-bed and matrix. The amount of nail to be taken varies some-

what according to the severity of the lesion, but as a rule it should remove a little more than a quarter of the visible area of the nail. A second incision along the paronychium is made to include removal of all the "reflected layer" to where it joins the matrix. This latter incision is carried proximally, diverting a little to the side to facilitate removal of the matrix from the corner of the nail-bed, and the matrix is removed from this area, cleaning down to the subungual space. If the nail matrix be not fully removed from the corner, a horn of nail will grow, requiring further removal. Fat and subcutaneous tissue beneath are evidence of complete removal. The paronychial and eponychial flaps are replaced. The obliquity of the original nail incision removes that part of the nail-bed which furnishes growth to the thin strip of nail distal to it. This strip will ultimately disappear, leaving nail-bed epithelium and a chisel edge to the nail. Epithelium from the paronychial edge will grow across the subungual space to meet the proliferating nail-bed epithelium.

A radical procedure is available in advanced cases where reasonable footwear will not be worn. It consists of removal of the whole nail-bed and the shortening of the great toe by removal of about half of its terminal phalanx. This procedure, though radical, is effective and sure in its results. The function of the great toe is not appreciably impaired and recovery is fairly rapid. Two longitudinal incisions are made, one on each side as a continuation of the lateral nail sulcus. These incisions reach almost to the interphalangeal joint. The flap of epithelium thus outlined is dissected proximally, just dorsal to the "reflected layer", until the junction is reached between the nail matrix and the "reflected layer". Here the dissection is carried deeply just proximal to the base of the matrix, to include the whole nail-bed, and is then carried distally in the subungual space until the distal end of the toe is reached. The whole nail, with its nail-bed, is thus removed, and great care must again be taken to remove the corners of the matrix. With bone snips the distal half of the phalanx is removed by a transverse cut. The soft parts of the toe distally now form a ventral flap, and its upper edge may be shaped to enable it to be brought backwards across the cut surface of the phalanx, to be stitched to the eponychial flap. Care must be taken that sufficient bone has been removed to allow this approximation without tension. As a rule redundant tissue on either side distally is best treated by a "V" excision with suture. The whole procedure is best carried out with a rubber tube tourniquet round the base of the great toe. A piece of sterile gauze soaked in equal parts of castor oil and friar's balsam may be applied over the area of operation, or a simple dry dressing may be used. In either case it is safe to leave open for inspection some small area of the toe distally. It is surprising what little trouble there is from infection when it is considered that there is free infection of the area at the time of operation. Similarly also, infection of the raw bone surface does not seem to occur.

Before these major operative procedures are performed rest and appropriate active measures for the diminution of the infection should be undertaken.

The problem of paronychia due to monilia infection must be borne in mind, and more properly belongs to the domain of the dermatologist. It is the cause of a definite proportion of cases. While I do not wish to encroach upon this domain, a few brief remarks are included here for completeness, culled from Robert W. MacKenna, "Diseases of the Skin", 1933:

> These yeast-like organisms, especially *Monilia pinoyi*, are more commonly found in woman than in man, and are more frequent in the hand than in the foot, and again, more often affect two or more nails.
>
> The avoidance of dirty orange sticks and of a soaked condition of the skin is of primary importance, and use is made of a fungicide. Where the nail is affected, avulsion and disinfection under a general anæsthetic are indicated.

S. H. Scougall, M.B. (Sydney),

Honorary Orthopædic Surgeon, Royal North Shore Hospital.

British Medical Association News.

SCIENTIFIC.

A meeting of the New South Wales Branch of the British Medical Association was held at the Sydney Hospital, Sydney, on October 19, 1933. The meeting took the form of a series of clinical demonstrations by members of the honorary staff. Parts of this report have been published in the issues of March 24 and 31, 1934.

Hyperplastic Inflammation of the Colon.

Dr. George Bell showed a female patient, aged sixteen years, who had been admitted to hospital on December 12, 1932, and discharged on February 20, 1933. At the time of admission she complained of pain in the epigastrium that had been persistent, with mild exacerbations, since August, 1932. Since September, 1932, she had had diarrhœa, passing about ten stools a day; she had also had complete amenorrhœa. Examination at that time revealed a mass, tender on pressure, in the right iliac fossa. The leucocytes numbered 16,720 per cubic millimetre. The pulse rate was 140 per minute, and the temperature was 37·6° C. (99·8° F.). There were physical signs of mitral stenosis. X ray examination after the administration of a barium enema revealed "extreme irritability of the caecum, suggesting an intense colitis, probably tuberculous". X ray examination of the chest revealed enlargement of the bronchial glands, otherwise nothing significant. Repeated examination of sputum and fæces did not reveal the presence of tubercle bacilli. There was no reaction to the Wassermann test. On January 18, 1933, ileo-colostomy was performed. The lower 12·5 centimetres (five inches) of the ileum, the ascending colon, the hepatic flexure and portion of the transverse colon were greatly thickened and inflamed. The appendix appeared free. Tubercles were not seen. The colon was not adherent to surrounding organs. This mobility of the colon would have rendered excision possible were it not for the cardiac lesion. Anastomosis of the ileum to the transverse colon was performed. The pulse rate after the operation varied from 120 to 150 per minute for five days.

On July 13, 1933, the patient was again seen; she was then looking well and had gained 19·8 kilograms (three stone and two pounds) in weight. At the time of the meeting her general condition was excellent.

Professor Harold Dew remarked that in these cases there seemed to be three distinct ætiological factors. There might be a hyperplastic fibrous tuberculosis, in which the tuberculous nature was at times hard to prove, particularly in comparatively fit people; there was little, if any, mucosal ulceration, most of the fibrotic thickening being in the wall and surrounding subperitoneal tissues; this occurred in young people as a rule, although no age was altogether exempt. Again, such a pericolitis might be due to the presence of small diverticula, which were often hard to find, the inflammation being low grade and non-specific, and liable to occasional subacute exacerbations. Professor Dew said that he believed there was a non-specific low grade inflammation of the colonic wall, which might go on to cause great thickening and fixation, almost to fibromatosis; certainly in some of these cases there appeared to be no evidence of tuberculosis. The caecum was commonly affected, and after that the descending colon and sigmoid colon. The best treatment would seem to be ileo-colostomy, to side-track the fæces and give the bowel as much rest as possible.

Ununited Fracture of the Right Tibia.

Dr. Bell's next patient was a man, aged twenty-four years, who had been admitted on September 19, 1932, and discharged on November 17, 1932. In June, 1931, he fractured both tibia and fibula of the right leg while playing football. He stated that he had been treated in back and side splints for eight weeks, then caliper for three months; he had walked with a stick since February, 1932. Examination at the time of admission revealed a

fusiform swelling at the site of fracture, and movement at the site of fracture of the tibia; there was no pain. There was no reaction to the Wassermann test. By X ray examination it was seen that the fibular fragments were firmly united, but that there was no bony union between the tibial fragments. On September 28, 1933, the fibrous tissue between the fragments was excised, the ends were scarified, and a massive sliding bone graft from the shaft of the fractured right tibia was inserted. The leg was then put in plaster. A plaster support was worn for some months and the patient was encouraged to bear weight on the affected limb. At a later date he was fitted with a caliper extending to immediately below the knee. At the time of the meeting there was excessive formation of bone at the site of the graft, and union was firm; the patient walked without difficulty or pain.

Carcinoma of the Male Breast.

Dr. Bell also showed a male patient, aged forty-two years, who had been admitted on February 20, 1933, and discharged on April 14, 1933. In August, 1931, he had first noticed a small lump in his right breast, which he thought had increased slightly in size. It was not painful and was about the size of a pea. He had been treated at the Prince of Wales Hospital for eight years for "gastric trouble". He stated that at one time his blood had reacted to the Wassermann test. Examination revealed a tumour in the superior lateral quadrant, about 2·5 centimetres (one inch) from the nipple of the right breast; it was hard and freely movable on the underlying tissue. On February 22, 1933, the nodule was excised under local anæsthesia. Dr. Keith Inglis examined the specimen and found scirrhous carcinoma; he expressed the opinion that the axillary glands should be removed. On March 15, 1933, radical amputation of the right breast was performed. The wound had healed by April 10, 1933. The patient had since been given deep X ray therapy. At the time of the meeting there was no sign of recurrence.

Dr. Bell remarked that the patient had complete range of movement at the shoulder joint; he was shown in order to demonstrate the free range of movement after the radical operation on a male.

Dental Cyst of the Mandible.

Dr. Bell's last patient was a woman, aged twenty-two years, who had been admitted on March 13, 1933, and discharged on May 12, 1933. In 1925 she had first noticed a swelling on the right side of the mandible; this had gradually increased in size. It was not painful. A tooth had been extracted from the site eleven years previously. Examination revealed an oval-shaped swelling on the medial and lateral aspect of the right mandible in the pre-molar and first molar region. It was not fixed to the surrounding tissues. The so-called egg-shell crackling was demonstrated by palpation. The thin shell of bone yielded to pressure like a thin layer of celluloid. X ray examination revealed a large cyst of the right mandible. The last two molar teeth projected into the cavity of the cyst, and it appeared that the mandible would fracture with very little violence. On March 22, 1933, the cyst was partially removed and the cavity curetted. The inferior dental nerve traversed the cavity and lay quite free in it; it was removed. The cavity was packed with iodoform gauze and liquid paraffin. Streptococci were cultured from the cyst contents. The pathological report was to the effect that the cyst was lined by squamous epithelium which showed considerable hyperplasia, but the overgrowth was presumably within benign limits. The patient reported again on October 12, 1933, feeling very well. At the time of the meeting she was well. The cavity had healed. A recent radiograph had revealed extensive regeneration of bone of the horizontal ramus of the mandible.

Pelvic Abscess.

Dr. H. S. Stacy showed a man, aged sixty-five years, who had complained of sudden pain around the umbilicus, of a colicky nature; it had persisted. Three days later he had taken a saline aperient and had then become affected with diarrhœa. Four to six days after the onset, the pain had settled in the right iliac fossa. The patient had vomited twice and had had a rigor. Examination at the time of admission revealed tenderness over the lower half of the abdomen, most marked in the right iliac fossa, where there was also rigidity. The leucocytes numbered 21,000 per cubic millimetre of blood. By rectal examination a tender mass could be felt on the right side of the pelvis. Blood was present on the gloved finger. The abdomen was opened by an incision at McBurney's point. The serous coat of the appendix was hyperæmic; otherwise the viscus was normal. The appendix was removed. There was free fluid in the abdomen. A cystic mass, which was leaking into the peritoneal cavity, was palpated in the pelvis. It was fixed to the pelvic colon and rectum. The abdominal wound was sewn up and the patient put in the lithotomy position. A bivalve speculum was inserted into the rectum and an incision was then made into the anterior rectal wall at the site of the mass about 6·25 centimetres (two and a half inches) from the anus, and Howard Kelly's forceps were introduced to dilate the incision. Pus flowed out; a rubber drainage tube was then inserted and stitched to the skin outside the anus. Five days later this tube was removed, the opening that was left being dilated by the finger every other day. Three and a half weeks later the patient was discharged well, with the cavity obliterated. X ray examination subsequently revealed some diverticula in the sigmoid region and some colitis of the descending colon.

Dr. Stacy remarked that the patient had had no symptoms referable to the diverticula either before or after the operation; so that he felt disinclined to follow the advice of a member to resect the affected portion of the sigmoid.

Fracture of the Leg.

Dr. Stacy's next patient was a girl, aged twelve years, who had fallen while skating and had fractured the left tibia in its lower one-third. The leg was fixed in a box splint, and five days later in plaster applied directly to the skin, from the forepart of the foot to above the knee, and a rubber heel pad was incorporated. By X ray examination it was observed that the lower one-third of the tibia was in good position. The patient began to walk seven days after the accident and was discharged on the eighth day. Subsequent X ray examination revealed good union and good alignment. The plaster was removed in the eighth week. The leg never developed the œdema that is such a common feature after prolonged rest and immobilization. There was no stiffness of the joints or wasting of the muscles of the limb. Naturally the unfractured fibula helped to splint the tibia.

Dr. Stacy pointed out that the function of the limb as shown at the meeting was perfect.

Dr. Stacy also showed a man, aged fifty-three years, who had been hit by a hammer on the lateral side of the leg and had sustained a fracture of the medial malleolus and the lower end of the fibula, causing slight lateral displacement of the foot. He was a heavy man. The day after the accident, under general anæsthesia, plaster was applied from the forepart of the foot to above the knee, the foot being placed in slight inversion. He walked five days after the accident. The leg was kept in this plaster splint for five weeks, then, with the foot quite straight, it was placed in another. In both cases the rubber heel pad was incorporated. The second plaster was kept on for three or four weeks. When it was removed, the joints were found to be free of stiffness; but there was some slight swelling around the angle. The patient walked quite well, and continued to do so. At the time of the meeting he was free of pain except in the forepart of the foot after exercise. The swelling had almost gone. It was then the thirteenth week after the accident. For three or four weeks he had been having hot air and massage treatment, together with swimming exercise.

Dr. Stacy remarked that he should be fit for light work in several weeks.

Visceroptosis.

Dr. Stacy also showed a woman, aged thirty-six years, who stated that she had been languid for eighteen months; the feeling of languor commenced at 9 a.m. and became progressively more pronounced as the day went on. She had lost 12·6 kilograms (twenty-eight pounds) in weight, and suffered from "dragging" pain in the right flank, extending to the groin, not related to food. She had had the pain for twelve months. For six months prior to admission she had noticed a lump in the right iliac fossa. She had suffered from dysuria and occasional nocturnal frequency of micturition for years, constipation for ten years, and almost constant dyspepsia, sometimes resulting in vomiting. Dr. Voss found at radiological examination that she had pronounced ptosis of the caecum and slight gastric hypotonicity; the duodenal cap was regular and mobile and there was no evidence of duodenal ileus.

The abdomen was opened by a grid-iron incision above McBurney's point. The caecum was found extremely mobile, atonic and distended, lying partly in the true pelvis. The liver was also noticed to be very low. The peritoneum was incised on the right lateral wall in a perpendicular direction, and the edges separated so as to leave portion of the wall devoid of peritoneum. The anterior edge of the incision was then sutured to the anterior band of the caecum, which had been lifted to this more elevated position. The patient had an uneventful recovery from the operation.

Dr. Stacy remarked that five months had elapsed since the operation, and the patient had completely lost her languor and her pain; she had no dyspepsia and no vomiting; she has not recovered her weight. By X ray examination on September 14, 1933, Dr. Cutler had found the caecum to be in good position. Several days later a pyelogram had been made by Dr. Bridge. This showed evidence of narrowing of the right ureter at the pelvi-ureteric junction. There was dilatation of the renal pelvis with slight clubbing of the calyces.

Neoplasms of the Urinary Tract.

DR. R. H. BRIDGE and DR. KEITH KIRKLAND showed a pathological specimen consisting of a primary papilloma of the lower end of the right ureter, which had caused, in addition to hæmaturia, a relatively rapid syndrome of obstruction with back-pressure on the kidney. (A more detailed report of this case appeared in the issue of this journal dated February 3, 1934.)

Dr. Bridge and Dr. Kirkland also showed a large hypernephroma of the upper pole of the left kidney, removed from a man, aged forty-three years. The retrograde pyelogram obtained in this case was shown. Dr. Bridge and Dr. Kirkland remarked that it was very disconcerting in that the only abnormality seen was a relative filling defect of the upper major calyx. The patient had been sick for less than a year, and he had sought advice only because of pain in the left flank. The lesson to be learnt was that every case of hæmaturia must be investigated immediately if cancer of the urinary tract was to be attacked at an operable stage.

Other neoplasms demonstrated by Dr. Bridge and Dr. Kirkland included a sarcoma of the kidney, a papillary carcinoma of the renal pelvis, and a renal carcinoma of a papilliferous structure somewhat resembling that of certain ovarian growths.

Congenital Abnormalities of the Urinary Tract.

Dr. Bridge and Dr. Kirkland also showed some specimens of congenital abnormalities, among which was a kidney with a double ureter and a bifid pelvis; the lower half of the pelvis drained renal tissue that was extensively aplasic. In another abnormal kidney there was aplasia of the upper half with undeveloped calyces; there were two ureters, one of which was ectopic and had caused lifelong incontinence, as the lower opening was in the urethra below the external sphincter.

Instruments.

Dr. Bridge and Dr. Kirkland also showed a Stern-McCarthy resectoscope for transurethral treatment of certain types of prostatism. The technique of its use was explained.

A recently modified bladder retractor was also shown. Dr. Bridge and Dr. Kirkland pointed out that the principle of fixed retraction, which was by no means new in abdominal and bladder surgery, was achieved by the use of adjustable blades fitted to a ring. The upper and two lateral blades had grooves for light-carriers, which incidentally were interchangeable and easily fixed into position by an ingenious locking screw. The modern operation of prostatectomy demanded visual inspection of the neck of the bladder for the toilet of the prostatic cavity, and it was asserted that with the use of this retractor the optimum exposure was obtained by a minimum of manipulation.

Multiple Pathological Fracture of the Upper End of the Humerus.

DR. R. V. GRAHAM and DR. JOHN HOETS showed a male patient, aged fifty-three years, who stated that his right shoulder had been injured by a fall one year previously. A radiograph had been taken at the time and he had been told that no osseous lesion had been found. Movements of the right shoulder had gradually become limited. On examination it was seen that the right deltoid was more prominent than the left; the supraspinatus and infraspinatus muscles on the right side were wasted; there was no muscle spasm; abduction and lateral rotation of the shoulder were limited. A radiograph revealed considerable deformity of the humerus, with numerous small transradiant areas, probably the end-results of an old osteomyelitis. There were two recent fractures of the humerus, one through the surgical neck and one about 6·25 centimetres (two and a half inches) distal to this, both of which were now firmly united. With the application of hot air and the institution of active movements the pain gradually lessened, but the range of movement was still limited. It was proposed to explore the upper end of the humerus at a subsequent date.

Lumbar Spondylitis with Compression Neuritis of the Lumbar Nerve Root.

Dr. Hoets and Dr. Graham also showed a male patient, aged sixty-nine years, who complained of pain in the back, which had commenced suddenly one and a half years previously. The pain had been referred down the right sciatic nerve. For one year there had been gradual loss of power in the right lower limb. On examination it was seen that there was no wasting; but there was a foot-drop on the right side; the knee jerk was exaggerated; there was no anæsthesia; the plantar reflex was normal. X ray examination revealed marked spondylitis in the lumbar spine with osteophytes almost uniting at the adjacent margins of the second and third lumbar vertebræ on the right side. It was proposed subsequently to remove these osteophytes.

Endocrine Dystrophy.

The next patient shown by Dr. Hoets and Dr. Graham was a girl, aged fourteen years, whose weight at birth had been 5·4 kilograms (twelve pounds). She had suffered from congenital club foot and dislocation of the right hip. She had been receiving treatment most of her life for her feet, hip and obesity at various hospitals. Her congenital deformities had never permitted normal activity. She had menstruated once at the age of twelve years, and twice only since, the last time six months previously. She had come under observation one month before the meeting, her main disability being her enormous size. Her weight was 130·5 kilograms (twenty stone ten pounds). X ray examination of the skull revealed no departure from normal. The basal metabolic rate at a first estimation appeared to be accelerated, and later slower than normal. The patient was mentally alert; her skin was soft and moist, and her hair and nails were normal in appearance. Her pulse rate was more rapid than normal. Her mother said that she had been treated by "glands" tablets for years without any check in the increase in her weight. One month before the meeting the adminis-

tration of thyreoid extract was commenced. She was given 0·18 gramme (three grains) a day at first; the dose was gradually increased to 0·42 gramme (seven grains) a day. During this time she had lost 4·0 kilograms (nine pounds) in weight, her sleep had become less troubled, and her breathing more comfortable.

There was considerable discussion on this case, the consensus of opinion being that she did not conform to any recognized type.

Kienbock's Disease.

Dr. Graham and Dr. Hoets next showed a patient, aged fifty years, who had been referred to the orthopædic department in December, 1932, for physiotherapy to the right wrist joint. X ray examination revealed nothing significant. The wrist was swollen and acutely painful; it was put at rest in plaster, and later a celluloid cast. The swelling and pain gradually subsided. X ray examination in June, 1933, still failed to reveal evidence of any pathological condition; but in September the report was that the condition was one of Kienbock's disease. Clinically the wrist was almost normal in appearance. There was considerable limitation of movement in all directions, but pain was almost absent. There was no history of injury previous to the onset of symptoms.

Occupational Therapy.

The occupational therapy room, a recent addition to the Department of Orthopædics, was open for inspection. Patients suffering from disabilities of the upper limbs were at work on chair-caning, plaiting, weaving *et cetera*.

Miss Uther Barker (Honorary Occupational Therapist) showed examples of work done by the patients.

Obituary.

THOMAS WILLIAM SHERLOCK MASON.

We regret to announce the death of Dr. Thomas William Sherlock Mason, which occurred on March 31, 1934, at Mosman, New South Wales.

ROBERT KINGSBURY LEE-BROWN.

We regret to announce the death of Dr. Robert Kingsbury Lee-Brown, which occurred on April 2, 1934, at Sydney, New South Wales.

Corrigendum.

Mr. G. V. Rudd writes that two errors have occurred in his paper appearing in the issue of March 31, 1934. In Table III the figure for hydrochloric acid in column 2 should be 0·0867; the figure for sodium in column 5 should be 0·0357.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser", pages xvi, xvii

Federal Council of the British Medical Association in Australia: General Secretary.

Launceston Public Hospital, Launceston, Tasmania: Resident Medical Officer (male).

Mental Diseases Hospital, New Norfolk, Tasmania: Junior Medical Officer.

Parramatta District Hospital, Parramatta, New South Wales: Junior Resident Medical Officer.

Rockhampton Hospital, Rockhampton, Queensland: Resident Medical Officer.

Sydney Hospital, Sydney, New South Wales: Honorary Officers.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
New South Wales: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
Victorian: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
Queensland: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Brisbane Associated Friendly Societies' Medical Institute. Chillagoe Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their agreement to the Council before signing. Lower Burdekin District Hospital, Ayr.
South Australian: Secretary, 207, North Terrace, Adelaide.	Combined Friendly Societies, Clarendon and Kangarilla districts. All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
Western Australian: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
New Zealand (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Editorial Notices.

Manuscripts forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary be stated.

All communications should be addressed to "The Editor", The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Subscription Rates.—Medical students and others not receiving The Medical Journal of Australia in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £3 for Australia and £2 5s. abroad *per annum* payable in advance.